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The American Heart Journal

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The American Heart Journal

VOL. 10 JUNE, 1935 NO. 5

Original Communications

CORONARY ARTERIOSCLEROSIS, CORONARY THROMBOSIS, AND THE RESULTING MYOCARDIAL CHANGES

AN EVALUATION OF THEIR RESPECTIVE CLINICAL PICTURES INCLUDING THE ELECTROCARDIOGRAPHIC RECORDS, BASED ON THE ANATOMICAL FINDINGS*†

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CHICAGO, ILL.

INTRODUCTION

THE work of Herrick[1] in 1912 stimulated the extensive study of angina pectoris and coronary thrombosis which has greatly expanded our knowledge in this field (cf. Levine and Brown,[2] Riesman and Harris[3]). Nevertheless it is recognized that many aspects are still unexplored (cf. Herrick,[4, 5] Karsner[6]). Most of the observations have been made on patients followed clinically over a long period of time, on serial electrocardiograms, or on necropsy material. There have been few attempts to correlate the details of the autopsy findings with the clinical and electrocardiographic data, other than the use of the autopsy material as a check on the clinical. It seemed to us that important information and a more appropriate perspective might be obtained if a group of cases, selected on the basis of the anatomical lesions by the pathologist without reference to the clinical or electrocardiographic findings, were analyzed and later correlated with the clinical data. In such an analysis, which starts with the post-mortem findings, there is the disadvantage that some of the cases selected may

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not have received sufficient clinical study from the cardiac angle. This disadvantage, however, is distinctly outweighed by the fact that such a group more nearly represents the average types encountered by the physician in general practice in patients between forty and seventy years of age.

Instead of trying to construct a composite pathological picture for a group of patients diagnosed clinically as angina pectoris or acute coronary occlusion, we have attempted to determine the clinical pictures and the electrocardiographic findings in a group of cases showing, at post-mortem examination, advanced coronary sclerosis, coronary thrombosis, and the resulting myocardial lesions.

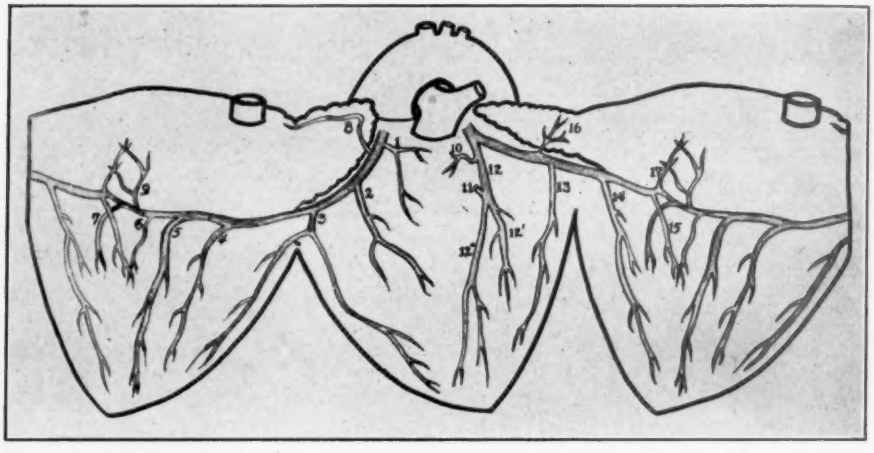

Fig. 1.—The distribution of the coronary arteries as found in 80 per cent of adult human hearts (over thirty years of age). (Adapted from Spalteholz.)

Branches of the Right Coronary Artery:
1. Arteria adiposa dextra.
2. Ramus ventriculi dextri anterior.
3. Ramus marginis acuti.
4. Ramus ventriculi dextri posterior.
5. Ramus sulci longitudinalis posterioris.
6. Ramus ventriculi sinistri posterior.
7. Ramus ventriculi sinistri posterior accessorius.
8. Ramus atrialis dexter anterior.
9. Ramus atrialis sinister posterior.

Branches of the Left Coronary Artery:
10. Arteria adiposa sinistra.
11. Arteria septi ventriculorum.
12. Ramus collateralis descendens anterior.
12′. Ramus primus. 12″. Ramus secundus.
13. Ramus ventriculi sinistri anterior.
14. Ramus marginis obtusi.
15. Ramus ventriculi sinistri posterior.
16. Ramus atrialis sinister anterior.
17. Ramus atrialis sinister posterior.

METHODS

Thirty-four cases comprised the material of this study which began at the necropsy table. Fresh hearts only were examined. In all hearts the branches of the coronary arteries were carefully dissected, as far as could be done with small scissors and inspected for their lesions. An attempt to inject the coronary vessels was abandoned because of the possibility of dislodging or losing recent thrombi. In every instance many blocks were cut from various portions of the heart including the infarcted areas. The sections were stained with

hematoxylin-eosin. When deemed necessary the van Gieson stain and a combination of iron-hematoxylin-orcein were used to reveal the presence of connective tissue and elastic fibers. Occasionally frozen sections were cut from the myocardium and stained with Sudan III to determine the presence of fat.

After the anatomical material had been studied, the clinical and electrocardiographic records were reviewed and the attempt was made to correlate these findings, with the lesions found at autopsy. In a study undertaken in this manner it is not surprising that only twenty-one patients had electrocardiograms.

In accordance with the manner in which the study was carried out, the pertinent autopsy findings in each case, not shown in the accompanying diagrams, are presented first. This is followed by an abstract of the clinical record and the pertinent electrocardiographic findings. This departure from the conventional method of presentation serves

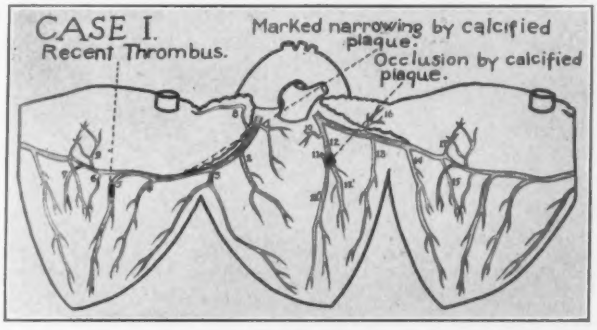

Fig. 2.

to emphasize the purely objective manner in which the studies were carried out. Each protocol is accompanied by a diagram of the heart showing the location and type of the coronary arterial lesions, and the location of myocardial infarcts, together with portions of the available electrocardiograms. The general discussion which follows is considered under the anatomical, clinical, and electrocardiographic divisions. The pertinent findings are also assembled in three tables.

CASE REPORTS*

CASE I.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 300 grams. The myocardium showed a diffuse fibrosis. The prostate revealed glandular hyperplasia.

Clinical Findings: Male, aged seventy-six years. The only significant history was a sudden attack of shortness of breath. Temperature was 98.2°, pulse 136, blood pressure 140/100, respirations 24 ("noisy respirations"). The lungs were emphysematous, liver and spleen were palpable; marked generalized arteriosclerosis

*The changes in the hearts are shown in the diagrams. The written descriptions have been omitted to conserve space.

and a moderately enlarged and firm prostate were found. The heart borders could not be percussed accurately because of the emphysema; the heart tones were faint. Laboratory examinations were not made. Diagnosis: Generalized arteriosclerosis; myocardial fibrosis; myocardial failure; emphysema; possible malignancy of prostate; senility; asthenia. The patient was acutely ill when admitted and died suddenly six hours later.

CASE II.—Myocardial aneurysm, "sudden" death.

Autopsy Findings: The heart weighed 625 grams. There was diffuse myocardial fibrosis. Nephrosclerosis of the arteriolar variety and carcinoma of the tail of the pancreas were also present.

Clinical Findings: Male, aged twenty-four years. Important points in the previous record were hypertension, albuminuria, angina pectoris of twelve years' duration, glycosuria for three years. The present complaint was the gradual develop-

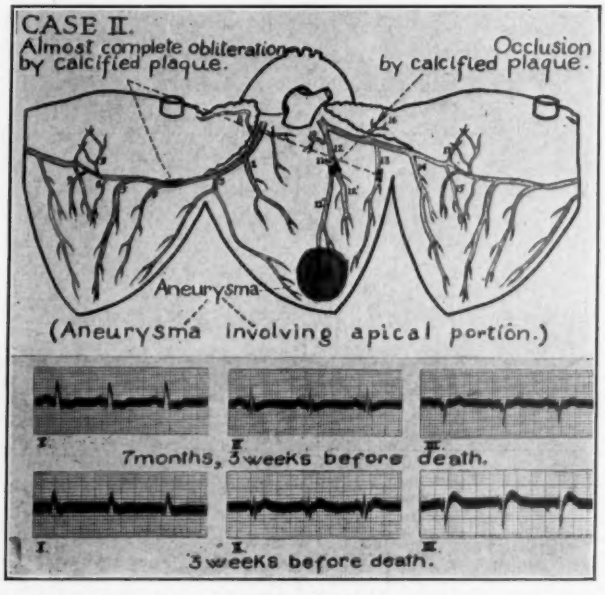

Fig. 3.—Case II. In this and subsequent records Leads I, II, and III read from left to right.

ment over a month of dyspnea, orthopnea, fatigue, anorexia, and diminished urine output. There was no precordial pain. Physical findings on (second) admission were: Blood pressure 150/98 (systolic readings of over 200 had been obtained at the previous admission); temperature 97.8°, pulse 80, respirations 24. The heart was enlarged to the right and left; heart tones were faint. Lung excursion was limited, and the resonance was impaired at the apices and bases. Bronchial breathing was found in the upper lobes, and râles at the left base. The liver was four fingerbreadths below the costal margin. No leucocyte count was made. The blood sugar readings were 219, 196, 139; CO_2 combining power 55; CO_2 content 53.8. Diagnosis: Generalized arteriosclerosis; myocardial fibrosis; cardiac hypertrophy; myocardial failure; pulmonary hyperemia; chronic glomerulonephritis; diabetes mellitus. Nineteen days after admission (three days before death) there was transitory syncope and death seemed imminent. There was no cardiac pain. On the twenty-second day, the patient got out of bed to use the bed pan on a chair. He fell from the chair to the floor and was found dead.

Electrocardiograms: The first record was made seventeen months prior to the second admission. The second record, made the day following the second admission and three weeks before death, showed nodal rhythm and left axis deviation. This record indicates myocardial involvement and intraventricular block. The changes between this and the previous record are compatible with a recent coronary occlusion.

CASE III.—Myocardial infarct, "sudden" death.

Autopsy Findings: The heart weighed 635 grams. There was also an acute serofibrinous pericarditis.

Clinical Findings: Male, aged seventy-three years. Two weeks before admission he experienced a sudden sharp severe pain in the abdomen, most marked in the epigastrium, which diminished after two to three hours. Two days previous to admission, he had a second attack associated with vertigo, and fell to the floor. There

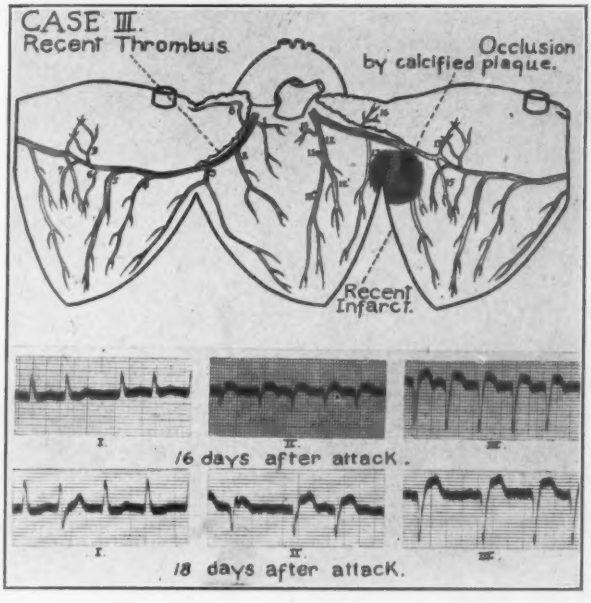

Fig. 4.

was marked dyspnea and the attack lasted fifteen to twenty minutes. Lower substernal pain, mild to moderate, was present between the two attacks, also some precordial distress. There was nausea, but no vomiting. No previous anginal or cardiac symptoms had been experienced. The previous blood pressure is not known. Wassermann and Kahn tests were negative. Physical findings on admission were: pulse 48, temperature 99.2°, respirations 24, blood pressure 126/66, white blood count 14,900. Generalized arteriosclerosis was present. The heart borders were 3.5 × 11 cm., tones were faint, and rhythm was regular. A friction rub was heard over the lower precordium. Breath sounds were distant, and a few râles were present in the lower right lobe posteriorly. The liver was 5 cm. below the costal margin. There was no edema of the ankles. Auricular fibrillation was noted the next day. A maximum temperature of 100.8° rectally was reached four days after admission. On the sixth day the pulse suddenly became weaker and more irregular. Cheyne-Stokes breathing and cyanosis developed; death occurred twelve minutes later. No immediate contributing factor was recorded. Diagnosis: Coronary thrombosis.

Electrocardiograms: Two records were made, one on the second, the other on the fourth day after admission. Both showed coarse auricular fibrillation, intraventricular block, occasional ventricular ectopic systoles, and left axis deviation.

CASE IV.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 400 grams. Diffuse myocardial fibrosis, bilateral bullous emphysema of the lungs, and multiple polyps of the stomach were also present.

Clinical Findings: Male, aged sixty-four years. Complaint: Sudden, nonradiating epigastric pain, "choking" in character, nausea and vomiting lasting ten hours, preceded by a cold sweat. The temperature was 98°, pulse 80, respirations were 32, blood pressure 80/60, white blood count 16,000. The temperature was not elevated at any time. The heart tones were barely audible, but there was no cardiac enlargement. The patient tried to get out of bed the morning after admission, and fell. He died an hour later. The epigastric pain was continuous from its onset and was only partially relieved by morphine. Diagnosis: Coronary thrombosis.

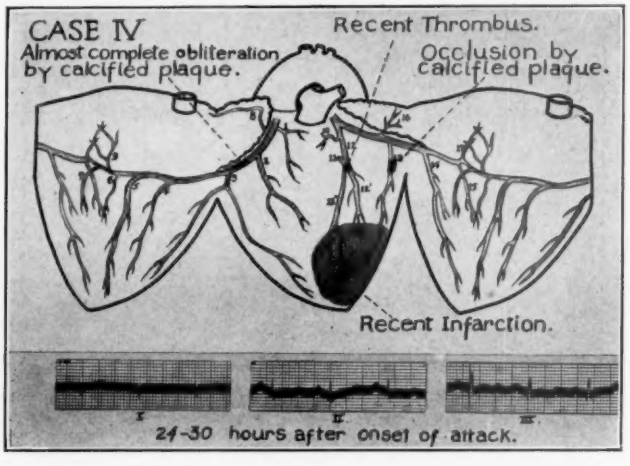

Fig. 5.

Electrocardiogram: An electrocardiogram was made about twenty-four to thirty hours after onset of symptoms. It showed sinus rhythm, QRS of low amplitude throughout, right axis deviation.

CASE V.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 400 grams. The myocardium was moderately fibrosed. An adenocarcinoma of the stomach and nephrosclerosis of the arteriolar variety, with arteriosclerotic scars of the kidneys ,were also present.

Clinical Findings: Male, aged sixty-eight years. He was brought to the hospital in an ambulance, moribund following a "heart attack," which had occurred shortly before admission. He was cyanotic, had labored breathing, cold extremities, and bloody sputum. Death occurred ten minutes after admission. No laboratory work was done. Diagnosis: Coronary thrombosis.

CASE VI.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 475 grams. Diffuse myocardial fibrosis, chronic caseous and fibrous tuberculosis of both lungs, and nephrosclerosis of the arteriolar variety were also noted.

Clinical Findings: Male, aged sixty-two years. The chief complaints concerned the genitourinary tract. There was also a history of severe pain in the left infraclavicular region, induced by exertion and radiating down the left arm to the elbow, and radiating to the left scapula, associated with a feeling of impending death. Physical Findings: Temperature 98°, pulse 80, respirations 22, blood pressure 134/96, white blood count 12,800. The heart was enlarged to the left; the heart tones were distant. Diagnosis: Hypertrophied prostate; angina pectoris; abscessed and thrombosed hemorrhoids. On the ninth day after admission, a prostatectomy was performed under spinal anesthesia. The postoperative course was uneventful and satisfactory until the third day (twelve days after admission) when he suddenly screamed, became cyanotic and pulseless, and died.

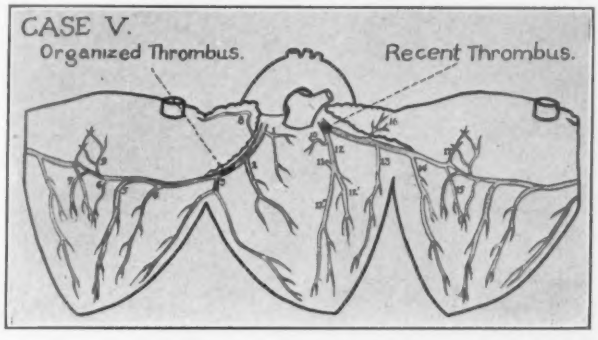

Fig. 6.

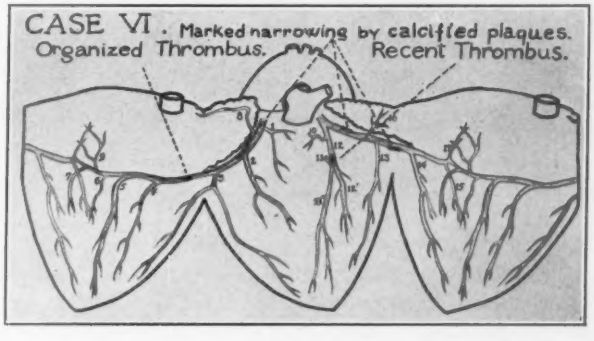

Fig. 7.

Case VII.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 400 grams. There was also a recent serofibrinous pericarditis. Multiple granulomas (gummas?) were present in the lung, and a recent bronchopneumonia. The prostate showed a marked glandular hyperplasia, and there was also a bilateral hydronephrosis.

Clinical Findings: Male, aged sixty-nine years. He was admitted to the hospital the second time principally because of symptoms referable to the lungs and the genitourinary system. The history was unreliable. The diagnosis at his previous admission was: Metastatic sarcoma of the lungs; hypertrophied prostate. At that time there was occasional precordial pain. At the time of the second admission the heart was enlarged to the left, and a soft apical systolic murmur was present over the apex. Blood pressure was 170/40 and 160/90; white blood count 18,000.

Diagnosis: Angina pectoris; metastatic sarcoma of the lung. Fifteen days after admission he gradually grew feebler. The heart tones gradually became weaker and the lips cyanotic. A choking spell occurred early in the afternoon, the pulse became irregular, and the patient suddenly succumbed.

Electrocardiogram: A record taken eight days before death showed sinus rhythm interrupted by occasional auricular ectopic systoles (not shown in the record), left axis deviation.

CASE VIII.—Myocardial infarction, "gradual" death.*

Autopsy Findings: The heart weighed 500 grams. There was generalized myocardial fibrosis. Mural thrombi were present in the right auricle and left ventricle, and multiple recent infarcts were found in both lungs, the spleen, and the kidneys. There was a generalized chronic passive hyperemia.

Clinical Findings: Female, aged fifty-six years. She was admitted because of cardiac failure. Two years previously she had complained of epigastric pain with nausea. At that time she had had weakness associated with numbness throughout the

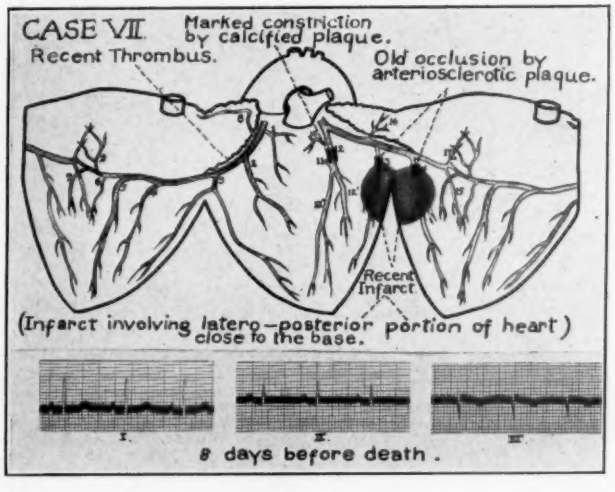

Fig. 8.

body. Four months before admission she had severe epigastric distress, nausea, and vomiting. An electrocardiogram was made two days after admission. Seven weeks after admission she experienced severe pain associated with tenderness in the left hypochondrium over the splenic area. There was profuse sweating, vomiting, fever, leucocytosis. At that time a second electrocardiogram was made. There was nothing during her stay in the hospital to indicate the occurrence of coronary occlusion.
Diagnosis: Pancarditis (acute); pneumonia.

Electrocardiograms: The second record shows sinus rhythm, interrupted by frequent ventricular ectopic systoles, first degree A-V block and intraventricular block.

CASE IX.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 450 grams. An acute serofibrinous pericarditis was also present.

Clinical Findings: Female, aged sixty years. A characteristic attack of severe anginal pain lasting one hour had occurred one year before admission. It was de-

*The term "gradual" death is used for brevity to indicate that the patient succumbed slowly.

scribed as a "hard squeezing sensation" located under the sternum, associated with exhaustion, but not with dyspnea. One and two days before admission, she had similar attacks which lasted longer, not relieved by rest or nitroglycerin. Temperature at that time was 98.6°, pulse 108. On admission the heart sounds were distant, and a friction rub was noted. Blood pressure varied from 126/102 to 182/110. Cyanosis was present. During the first day in the hospital she had pain under the sternum, which increased steadily. Gallop rhythm developed, and the blood pressure fell to 130/82. The white blood count on the day of admission was 9,300, on the second day 24,000. Temperature on entrance was 101.4°, the next day 102.2°. On the sixth day, just before she died she complained of an increase in the severity of the constant epigastric pain. Diagnosis: Coronary occlusion; angina pectoris; myocardial infarction.

Electrocardiograms: The first record shows sinus rhythm, intraventricular block

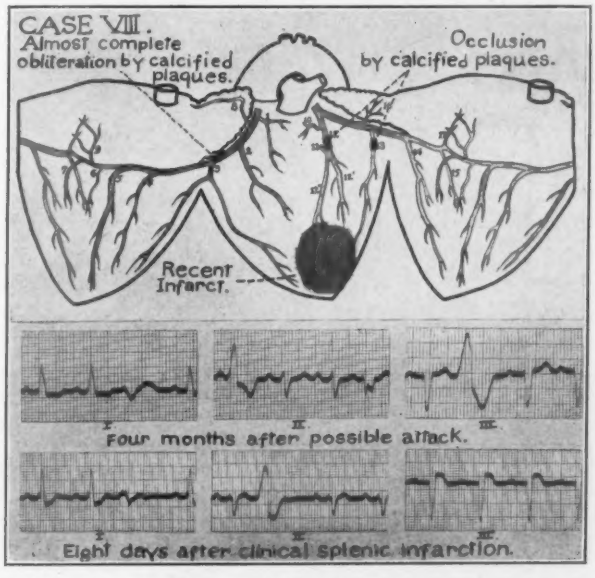

Fig. 9.—Case VIII. Electrocardiogram No. 2 taken twelve days before death (seven weeks after first record).

of the common bundle-branch type. The second record shows sinus rhythm, interrupted by paroxysms of auricular flutter with 2:1 and 4:1 conduction. The intraventricular block is unchanged.

Case X.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 475 grams. Cholelithiasis was also found.

Clinical Findings: Male, aged fifty-one years. Complaints were difficulty in walking for nine years, bladder trouble for three months, bloody stools for seven years. There were no cardiac symptoms. Except for increased aortic dullness, no abnormal cardiac findings were noted. Blood pressure was not recorded. The white blood count was 10,000. Diagnosis: Tabes dorsalis, hypertrophy of the prostate. A prostatectomy was performed under spinal anesthesia three months after admission. Sixteen days later an increase in cardiac dullness was noted. The heart tone became faint. A marked secondary anemia developed. Four months after admission the patient had a chill followed by temperature of 101°. The pulse became weak and thready, and there was a cold sweat but no cardiac pain.

CASE XI.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 525 grams. There were mural thrombi in the right and left ventricles and multiple pulmonary infarcts. A bronchopneumonia was also present.

Clinical Findings: Male, aged sixty-two years. Forty-eight hours prior to admission and following hard manual labor (shoveling coal), he had an acute attack

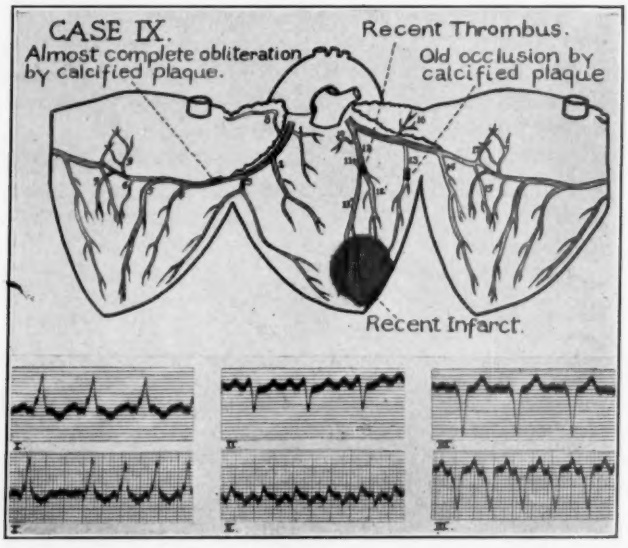

Fig. 10.—Case IX. Electrocardiogram No. 1 taken forty-eight hours after first clinical attack. Electrocardiogram No. 2 taken five days after first clinical attack, two days after second clinical attack.

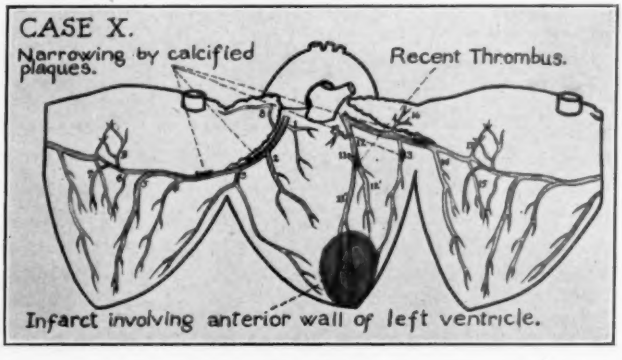

Fig. 11.

of severe dyspnea lasting five minutes. He had another the following day. There was cough and diffuse chest pain, which were attributed to a change in the weather. Physical Findings: Pulse 140, irregular; temperature 99.4°, blood pressure 160/108, white blood count 14,300. The patient was cyanotic and semistuporous. The heart was enlarged to the right and left; the chest was filled with crepitant and subcrepitant râles; breath sounds were impaired. Tentative diagnosis on admission: Bronchopneumonia. Three days after admission there was an attack of dyspnea, cyanosis, coughing, associated with pallor and sweating. The temperature was

102.4°, pulse 108, respirations 26; blood pressure on three occasions was 140/100, 120/90 and 140/100. Final diagnosis: Recent pulmonary infarction; enlarged and dilated failing heart (probably old hypertensive and coronary sclerotic heart), possible coronary thrombosis. There was no record of cardiac pain.

Electrocardiogram: The record shows sinus rhythm, left axis deviation, and occasional ectopic systoles arising from two ventricular foci.

CASE XII.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 450 grams. Mural thrombi were present in the left ventricle, and old and recent infarcts in the spleen and kidneys. A recent encephalomalacia was also noted.

Clinical Findings: Male, aged forty-five years. He had a sudden onset of complete left hemiplegia the night before admission. There was a history of two similar attacks one year ago, one on the right and one on the left side. Cardiac

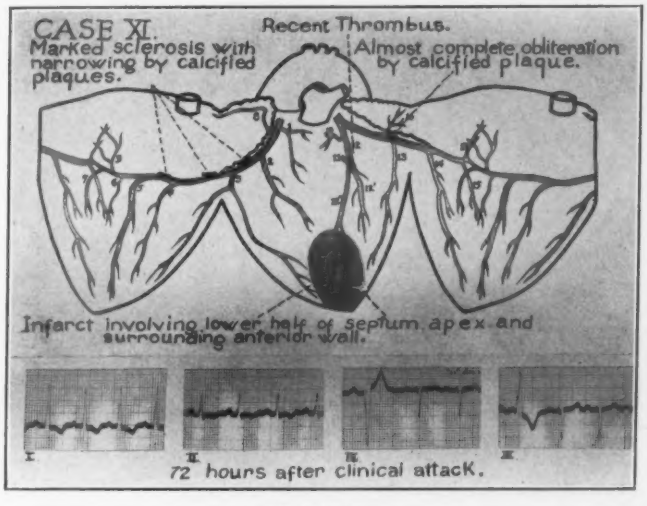

Fig. 12.

symptoms consisted only of slight dyspnea. Epigastric pain had been present for four years. The heart was enlarged to the right and left, rate 90. There was an occasional extrasystole; tones were distant and of poor quality. Blood pressure 115/70. White blood count 9,500. Diagnosis: Left hemiplegia; organic heart disease with hypertrophy and dilatation; coronary sclerosis. Four and one-half weeks after admission, the patient had a severe pain in the right chest lasting several hours. White blood count was 15,000. Blood pressure rose to 122 and then fell to 102 systolic; the pulse was thready; and there were extrasystoles. Diagnosis: Coronary thrombosis. Two days later he had pain in the left upper quadrant. At five the following morning, an attack of severe precordial pain was felt, and the patient died suddenly.

Electrocardiograms: The first electrocardiogram was made twelve days after admission; the second, shortly after the attack of right chest pain; the third, two days later before the attack of left upper quadrant pain. The first record shows sinus rhythm. The second and third records were similar to the first with the addition of frequent auricular ectopic impulses.

CASE XIII.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 450 grams. Mural thrombi in the left ventricle and an acute pericarditis corresponding to the infarcted area were also present. There was also a nephrosclerosis of the arteriolar variety.

Clinical Findings: Male, aged seventy-six years. Symptoms: Pain in the left elbow radiating to shoulder and precordium and left scapular angle; twelve to fifteen attacks over a period of approximately five weeks before death. Ten days before death, he had an attack lasting four hours; two days previous to death, one lasting three hours. The last attack began at 2 A.M. and death occurred at 8:30 P.M. **Diagnosis:** Coronary thrombosis.

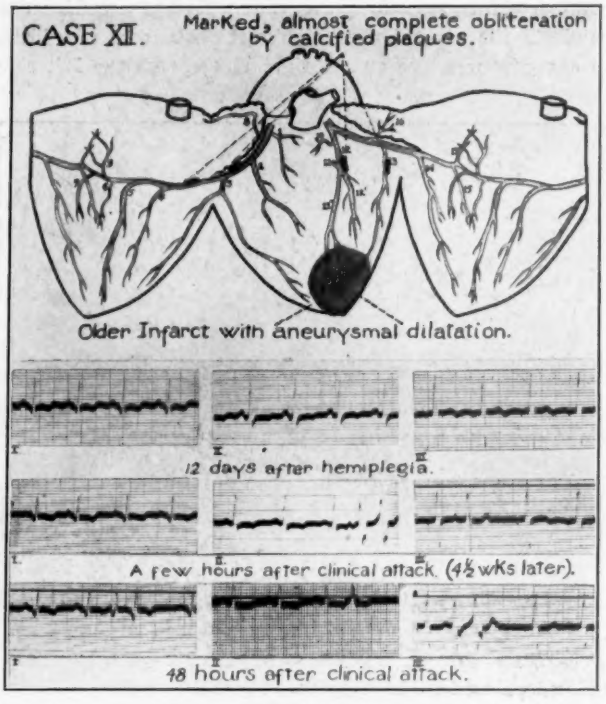

Fig. 13.

Electrocardiograms: The first record shows sinus rhythm, left axis deviation. The second record shows reversal of T_2 and T_3, and decrease in the size of T_1. QRS is smaller and the T type is indeterminate. The third record shows T isoelectric in Lead I, and smaller in Leads II and III. The fourth record shows T still smaller in Leads II and III. In the fifth record slurring of QRS appears in Lead I, and the duration is slightly increased in all leads. A small Q_1 is present and S-T is elevated in Lead III. The sixth record shows T inverted in Lead I; S-T has an upward convexity in Lead I and is elevated in Leads II and III. The seventh record is similar to the sixth except that the Q_1 tends to disappear, and the left axis deviation is increased.

CASE XIV.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 275 grams. There was a diffuse myocardial fibrosis. Associated findings were: Primary adenocarcinoma of the fundus

of the gallbladder with metastases to the peritoneal lymph nodes, to the peritoneum and liver; cholelithiasis and marked jaundice.

Clinical Findings: Female, aged fifty-eight years. Symptoms: Vague epigastric distress radiating to the left shoulder, associated with nausea and vomiting, syncope, angor animi lasting thirty minutes. The electrocardiogram was taken at this time.

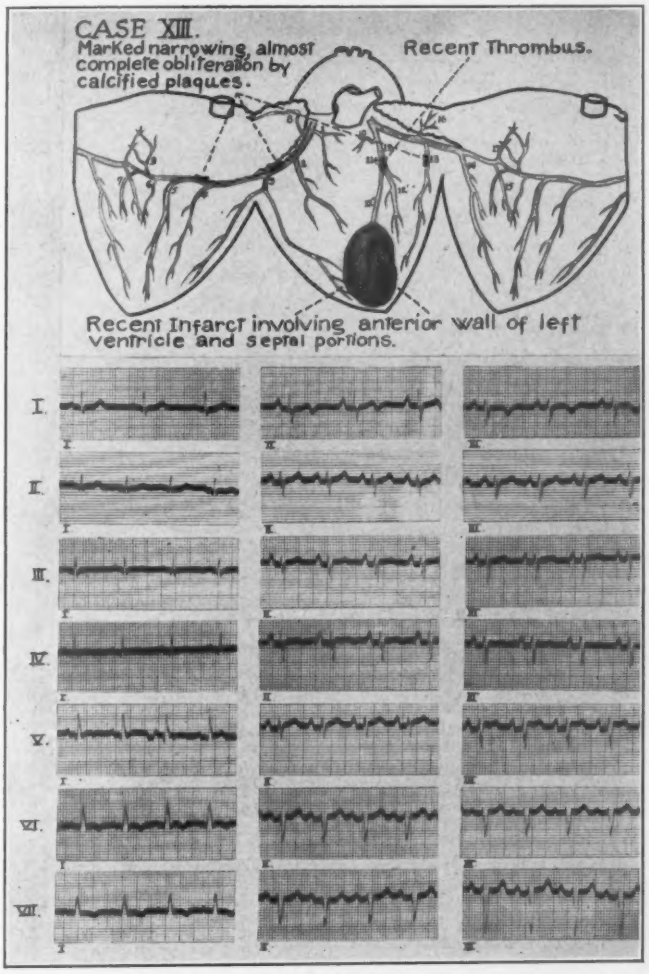

Fig. 14.—Case XIII. Electrocardiogram No. 1 taken three days after admission, three weeks after onset of symptoms. Electrocardiogram No. 2 taken twenty-four hours later and a few hours after an attack of pain lasting four hours. Electrocardiogram No. 3 taken two days after No. 2. Electrocardiogram No. 4 taken four days after No. 2. Electrocardiogram No. 5 taken six days after No. 2 and almost immediately after an attack of pain lasting one hour. Electrocardiogram No. 6 taken forty-eight hours after No. 5 and shortly after an attack of pain lasting two hours. Electrocardiogram No. 7 taken forty-eight hours after No. 5 and less than twenty-four hours after an attack lasting six hours. Patient died the same day.

Diagnosis: Chronic cholecystitis; myocardial fibrosis. Five and one-half months after this attack she was operated on for gallbladder disease under spinal anesthesia and died suddenly on the operating table.

Electrocardiogram: The record shows sinus arrhythmia.

CASE XV.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 375 grams. There were also a diffuse myocardial fibrosis and a recent fibrinous pericarditis. A mucinous adenocarcinoma of the pyloric portion of the stomach, with metastases to the peritoneal nodes, a chronic cholecystitis and a cholelithiasis were also found.

Clinical Findings: Female, aged seventy-five years. Complaints: Indigestion of four months' duration, anorexia for five weeks, epigastric distress and belching

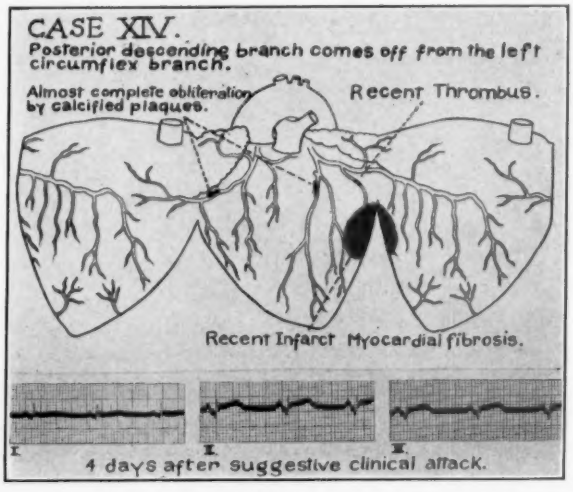

Fig. 15.

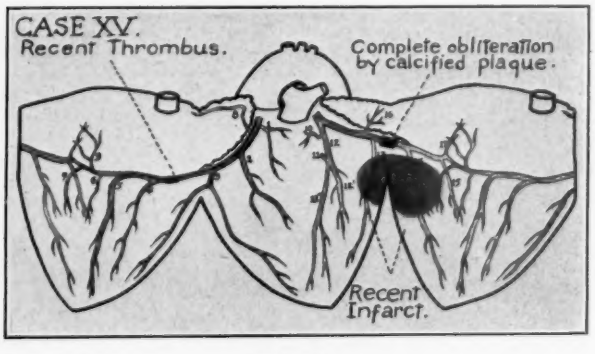

Fig. 16.

for weeks. There were no cardiac symptoms. On physical examination, the heart was enlarged to the right and left; heart tones were faint. A systolic murmur was heard over the entire precordium, best at the base. Blood pressure was 144/88, pulse 84. A mass was palpated in the epigastrium. X-ray examination revealed carcinoma of the pylorus and a "pathological" gallbladder. White blood count was 7,900. Ten days after admission the patient passed a large black fluid stool with free blood. This was followed by abdominal pain, weak rapid thready pulse, pulmonary edema, inaudible heart tones, and semiconsciousness. She died six hours later. Diagnosis: Coronary sclerosis; arteriosclerosis; possible carcinoma of the stomach.

CASE XVI.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 500 grams. There were mural thrombi in the left ventricle and an early fibrinous pericarditis. Old and recent infarcts were present in the left kidney. A recent encephalomalacia, nephrosclerosis of the arteriolar variety, and glandular hyperplasia of the prostate were also found.

Clinical Findings: Male, aged seventy-five years. He was admitted to the hospital in a comatose condition. The objective findings were: Cyanosis, Cheyne-Stokes respiration, pinpoint pupils. The heart tones were distant; there was gallop rhythm, rate 130. Blood pressure was 130/80, temperature 101.2°, respirations 32. A complete paralysis of the left eyelid and flaccid paralysis of the left side were present. Diagnosis: Left hemiplegia; arteriosclerosis; chronic myocardial fibrosis with moderate heart failure; pulmonary emphysema. Death occurred seven hours after admission.

CASE XVII.—Myocardial fibrosis, "gradual" death.

Autopsy Findings: The heart weighed 400 grams. There was myocardial fibrosis, but no infarct. A bronchopneumonia was present, in addition to a nephrosclerosis of the arteriolar variety.

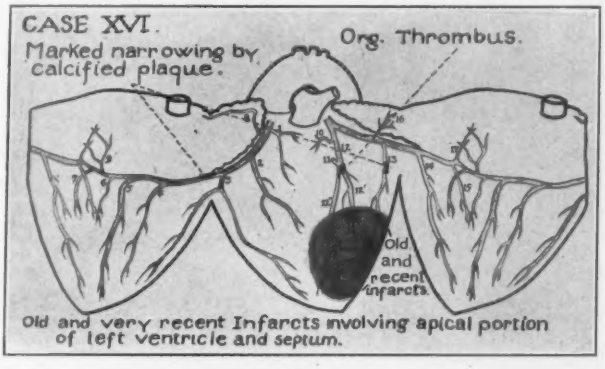

Fig. 17.

Clinical Findings: Female, aged seventy-six years. Complaints: Cough, weakness, dyspnea, bloody sputum for four days, and fever for two days. Physical findings: Pulse 140, respirations 38, temperature 103°. There were dyspnea and cyanosis. Heart borders were 3 × 13 cm. A loud, harsh apical systolic murmur was heard. No blood pressure was recorded. There were signs of a bronchopneumonia. White blood count was 34,000. Diagnosis: Bronchopneumonia; arteriosclerosis; probable coronary sclerosis; and nephrosclerosis. The patient gradually became weaker and died. At a previous admission, two months before, her complaints had been epigastric pain for five to six years, pain in the right upper quadrant radiating to shoulder for two weeks, palpitation for three weeks, and dyspnea for two years. The pain in the epigastrium and in the right upper quadrant was characteristic of gallbladder disease. There was no history of precordial pain. The heart was enlarged. There was a systolic murmur over the precordium (apex and aorta). The blood pressure was 235/105 and 175/80. X-ray examination showed a dilated thoracic aorta, and there was evidence of diverticulosis in the gastrointestinal tract. Diagnosis: Senility; arteriosclerosis; myocardial fibrosis.

Electrocardiogram: (Made at time of first admission.) It shows sinus rhythm and left axis deviation.

CASE XVIII.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 450 grams. There were mural thrombi in the left ventricle and in the right auricle, an anemic infarct in the left kidney, and a small area of encephalomalacia in the region of the left caudate nucleus. There was also a nephrosclerosis of the arteriolar variety.

Clinical Findings: Male, aged forty-nine years. Complaints: Precordial "pressure" pain for five years induced by exertion; short attacks of dyspnea and palpitation. During the five-year period he had one attack of precordial pain with restlessness, vomiting and pulmonary edema lasting for twelve hours. Subsequently there were similar attacks at long intervals. He died suddenly, after vomiting. Diagnosis: Coronary thrombosis; myocardial infarction.

Electrocardiograms: The first record made five years before death showed only left axis deviation. The second record showed inverted T_2 and T_3, positive $S\text{-}T_3$, small Q_1 and a depressed $S\text{-}T_1$. The third record a year later again resembled the first record. The fourth and fifth records show the changes one might expect from pro-

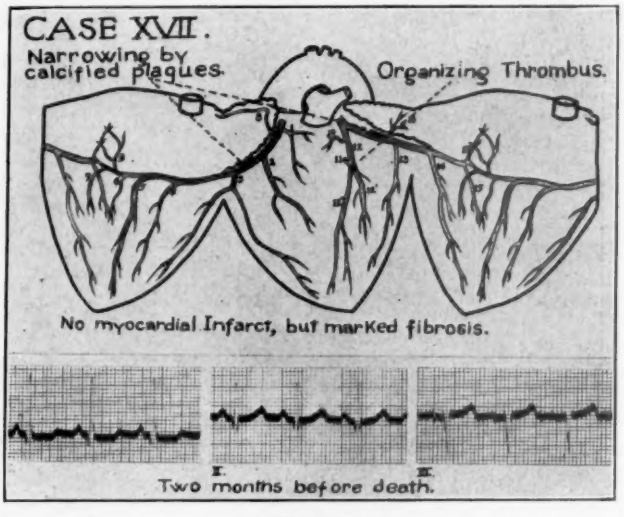

Fig. 18.

gressive myocardial fibrosis. The sixth record shows a reversal of T_3 and the development of a positive T_1 with persistence of the negative $S\text{-}T_1$ and $S\text{-}T_2$. Records 4 and 6 show ventricular ectopic beats.

CASE XIX.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 450 grams. There was also found a chronic peritonitis with formation of fibrous bands, a marked distention of the large and small intestines, and a circumscribed acute fibropurulent peritonitis.

Clinical Findings: Male, aged seventy-four years. Complaints: Complete obstipation, and pain just below the umbilicus for three days. Physical examination revealed a heart enlarged to the left and down. The abdomen was distended and tympanitic. There was a sausage-shaped mass on either side, and tenderness at the midline just below the umbilicus. Temperature was 98.8°, pulse 100, blood pressure not recorded, respirations 28. White blood count 10,400. X-ray examination revealed complete obstruction of the rectosigmoid, the cause of which could not be determined. Diagnosis: Intestinal obstruction; acute peritonitis. An ileostomy was performed under ethylene anesthesia. After four days of uneventful postoperative

recovery, he became weak and died the same day. There was nothing in the preceding history or postoperative course to indicate coronary thrombosis.

CASE XX.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 400 grams. There was also an acute serofibrinous pericarditis with evidence of organization. Mural thrombi were present in the right auricle, and recent infarcts were found in both lower lobes of the lungs. There was also a marked glandular hyperplasia of the prostate.

Clinical Findings: Male, aged sixty years. Complaints: Severe substernal pain lasting nine hours, associated with fall in blood pressure, followed by fever, leucocytosis. Sixteen days later he sat up on the edge of the bed to use the urinal,

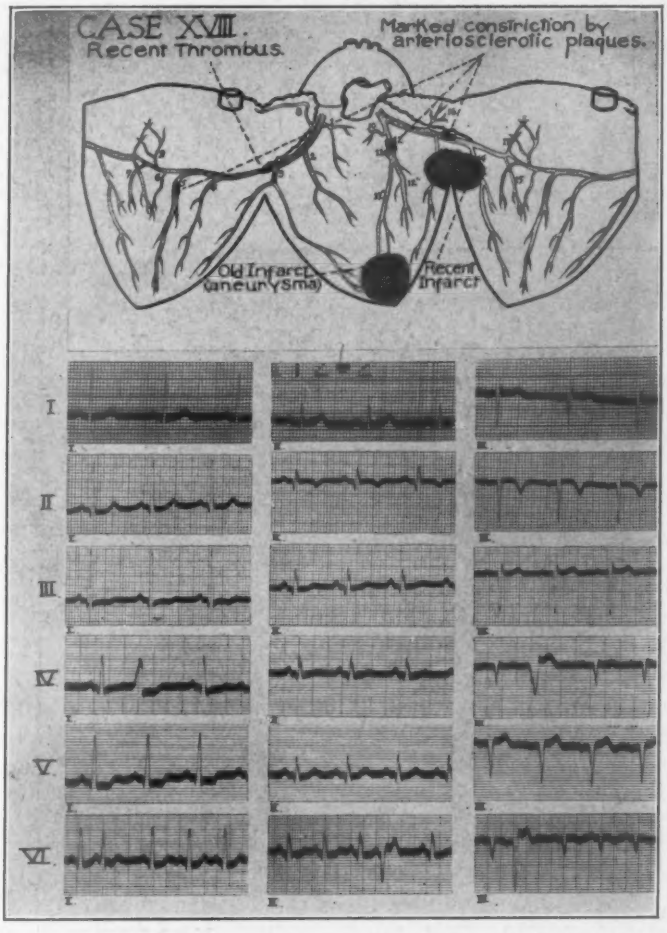

Fig. 19.—Case XVIII. Electrocardiogram No. 1 taken October 12, 1925, before onset of symptoms. Electrocardiogram No. 2 taken March 1, 1929, three years after onset of anginal symptoms. Electrocardiogram No. 3 taken May 12, 1930, shortly after onset of attacks of dyspnea coming on without warning and lasting all day. Electrocardiogram No. 4 taken September 26, 1930, four days before hospital admission; no change in symptoms. Electrocardiogram No. 5 taken October 11, 1930, sixteen hours after "cerebral" accident, ten days after attack of chest pain followed by bloody sputum and signs of pulmonary consolidation; attack diagnosed as coronary thrombosis with mural thrombi and cerebral and pulmonary emboli. Electrocardiogram No. 6 taken November 28, 1930, seventeen days before death and four days after attack of dyspnea, pain in chest, frothy sputum, nausea, followed by fever.

was seized with severe retrosternal pain and died instantly. Diagnosis: Coronary thrombosis; pulmonary infarction.

Electrocardiograms: The first record is within normal limits. The second record shows sinus tachycardia, small negative T_2, large negative T_2, and lower amplitude of QRS. The third record resembles the second.

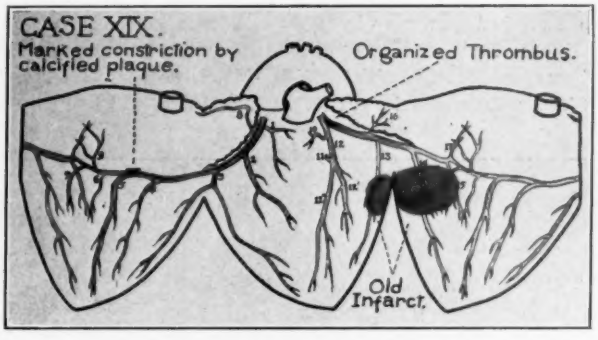

Fig. 20.

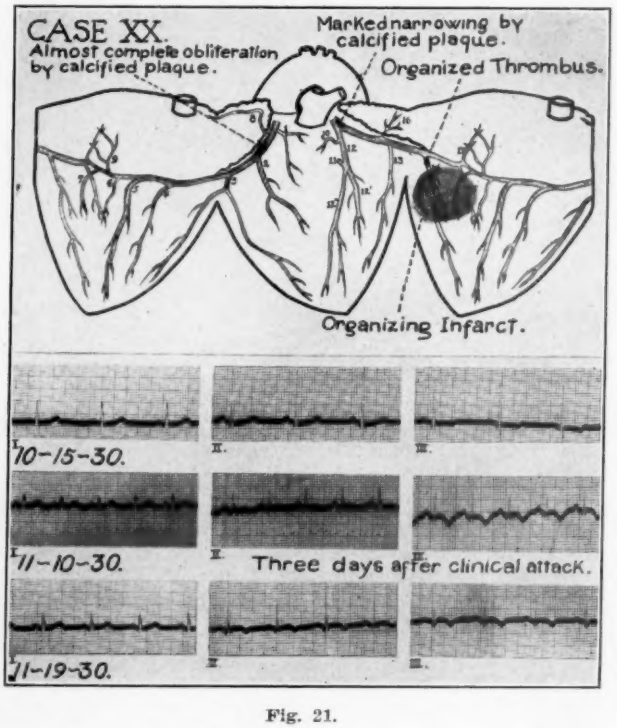

Fig. 21.

Case XXI.—Myocardial infarction (rupture of heart), "sudden" death.

Autopsy Findings: The heart weighed 375 grams. A recent infarct was present in the apical portion of the left ventricle, which had led to rupture of the heart at that point, resulting in hemopericardium. There was a very early nephrosclerosis of the arteriolar variety and an early Laennec's cirrhosis. Vascular

syphilis, diagnosed clinically, could not be verified at the autopsy. (The brain could not be examined.)

Clinical Findings: Male, aged sixty-seven years. Forty-eight hours before admission he had a sudden agonizing substernal pain radiating down the inner surfaces of both arms and into the head. This was accompanied by cold clammy sweat. Temperature was 100.4°, pulse 104, blood pressure 110/70 (had been 140/80); white blood count 29,900. The heart was enlarged, tones were distant, and extrasystoles were present. His cardiac condition improved until three days after admission when he complained of severe substernal pain, grunted, and died. There was previous clinical evidence of vascular and neurosyphilis, cirrhotic liver, ascites, encephalopathy with cerebellar ataxia prior to present admission. Diagnosis: Coronary thrombosis.

CASE XXII.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 450 grams. Additional findings were an old pericarditis, old infarcts in the spleen and both kidneys, purulent bronchitis, and bronchopneumonia.

Clinical Findings: Male, aged seventy-seven years. Only a meager history was obtainable. He had had heart trouble for four years. The present attack started

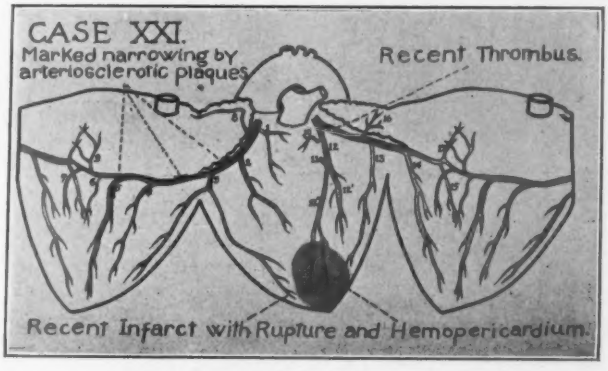

Fig. 22.

several weeks before admission. There was no history of pain. Cough, dyspnea, orthopnea, Cheyne-Stokes respiration, edema of the feet and ankles were present. The pulse was 92, temperature 99°, respirations 28, blood pressure 210/110, white blood count 18,200. There were audible rhonchi. Pulmonary resonance was impaired at both bases; fine and coarse moist rôles were heard throughout. Heart borders were 13.5 × 4 cm. The tones were of good quality, and the rhythm was totally irregular. There were no murmurs or friction rub. The liver extended two fingerbreadths below the costal margin. Ascites and edema of the feet and ankles were present. Blood sugar was 148, N.P.N. 63. Diagnosis: Myocardial degeneration on a hypertensive or arteriosclerotic basis; auricular fibrillation; coronary sclerosis; possible coronary thrombosis.

CASE XXIII.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 500 grams. A bronchopneumonia was also present.

Clinical Findings: Male, aged sixty-seven years. Complaints: Frequent attacks of substernal pain for the last two years. At the time of admission, these occurred daily. The pain radiated to both scapulae and down both arms, lasting minutes to hours and disappearing rather rapidly. Temperature on admission was normal, but

105.4° on day of death. Blood pressure was 194/124 and 204/124; white blood count 23,000 and 19,650. Two days later blood pressure was 130/80, and the patient had chest pain. The clinical course was progressively downward until death on the fifth day after admission. An electrocardiogram had been made six months previously. At this time he had had attacks of substernal pain radiating to the left chest, lasting from a few seconds to three hours. There was also pain in the left forearm. White blood count at that time was 14,800, blood pressure 165/106 and 128/84.

Electrocardiogram: The record shows sinus rhythm, first degree A-V block.

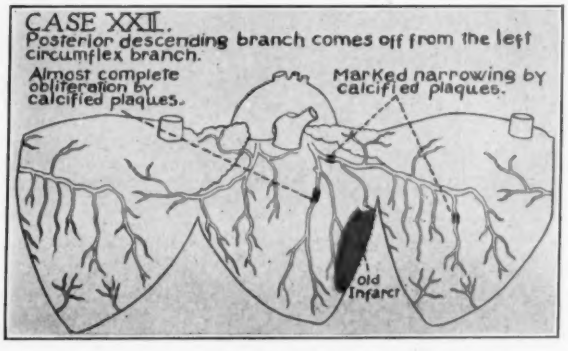

Fig. 23.

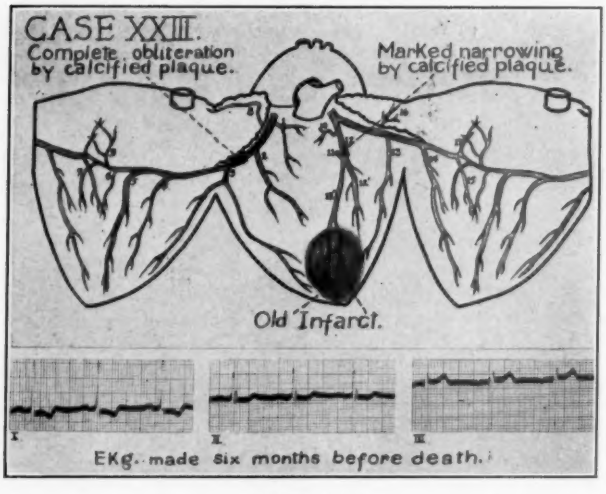

Fig. 24.

Case XXIV.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 600 grams. Mural thrombi were found in both ventricles. A circumscribed organizing pericarditis was also present. Additional findings were multiple infarcts of both lungs, chronic cholecystitis, and multiple adenomatous polyps of the colon.

Clinical Findings: Male, aged fifty years. Complaints: Pain in the midsternal region radiating to the back of two months' duration. He had had two previous attacks. The physical findings were those of pulmonary emboli and infarcts. Blood

pressure varied from 160/100 to 124/104; white blood count 10,600 to 15,900. Temperature on admission was normal, later 102.2°. The patient experienced progressive weakness, and death occurred twenty-seven days after admission. An electrocardiogram had been taken three months before admission. Diagnosis: Coronary thrombosis; pulmonary infarction.

Electrocardiogram: The record shows sinus tachycardia, left axis deviation.

CASE XXV.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 500 grams. There was a circumscribed organizing pericarditis. Mural thrombi were present in the left ventricle at the site of the infarct and also in the right auricle. Infarcts were found in the lower lobe of the right lung. There was an old fibrous tuberculosis of the upper lobe of the left lung, with marked bronchiectasis. Nephrosclerosis of the arteriolar variety was also present.

Clinical Findings: Male, aged seventy-two years. Complaints: Thirteen years ago following influenza he had more or less persistent precordial pain lasting two

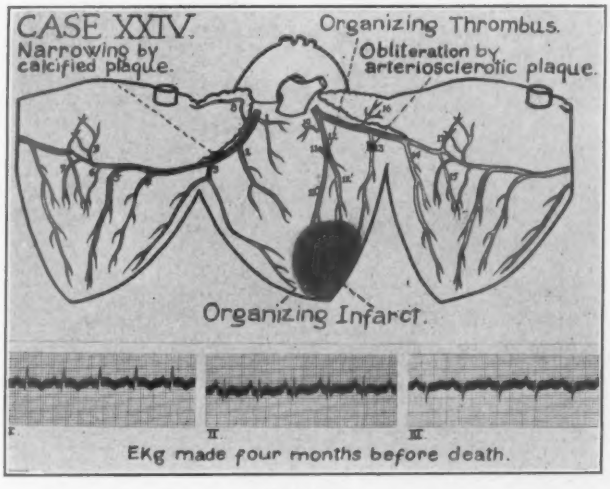

Fig. 25.

to three years. There had been occasional attacks of very severe pain ever since. Ten days before admission he had a sudden attack of dyspnea following a meal. Edema of the ankles developed three days later. There was a sense of constriction in the throat. Temperature was 97°, blood pressure 125/80; white blood count 12,800 on admission. On the fourth day at 8 A.M. the patient became restless and had a clammy sweat. He died suddenly at midnight while asleep. Diagnosis: Coronary thrombosis; rupture of the heart.

Electrocardiogram: The record shows sinus rhythm, QRS of low amplitude throughout.

CASE XXVI.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 350 grams. There was an organizing serofibrinous pericarditis.

Clinical Findings: Male, aged forty-eight years. Complaints: Substernal pain and constriction of two and one-half days' duration, unrelieved by morphine. Diabetes mellitus and anginal attacks four years ago were also mentioned. Blood pressure was 150/95; white blood count was 19,400. Temperature on admission

was 97.4°, later rising to 100.6°. Nine days after admission there was an attack of substernal pain, relieved by morphine; blood pressure was 130/90. The next day he had a similar attack; blood pressure fell to 110/60, pulse was 150, blood sugar 239. The heart showed signs of progressive failure, and he died the same day. Diagnosis: Coronary thrombosis; diabetes mellitus.

Electrocardiograms: The first record shows sinus tachycardia, right axis deviation, intraventricular block. The second record shows increased amplitude of QRS_1, S_2 and Q_3 are deeper, $S\text{-}T_3$ take-off slightly below the isoelectric level, QRS_3 is notched and T_3 is upright. The third record shows a decrease in the degree of right axis deviation. The amplitude of all deflections is less, $S\text{-}T_3$ is definitely depressed and T_3 is inverted.

Case XXVII.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 375 grams. An adenocarcinoma of the sigmoid with infiltration of the surrounding pericolic tissue and a small perforation were also disclosed at autopsy. There was a circumscribed fibrinopurulent peritonitis.

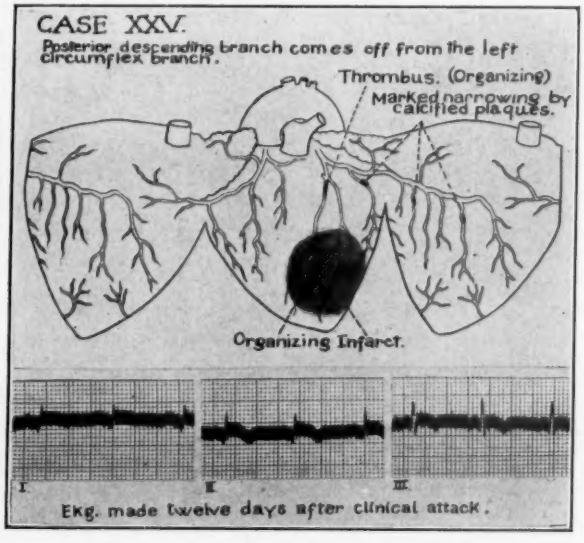

Fig. 26.

Clinical Findings: Male, aged seventy years. Complaints: Pain in the abdomen and vomiting of one day's duration. Absolute obstipation four days. He had had intestinal obstruction one year previous, relieved without surgery. There was no pertinent cardiovascular history, but he had taken digitalis for one year, and had had asthma for several years. On physical examination, the pulse was 130, temperature 101°, respirations 28; blood pressure was not taken; white blood count was 16,700. The heart was negative except for faint heart tones. The abdomen was distended, rigid, tender. Diagnosis: Intestinal obstruction, peritonitis, chronic asthma with cardiac involvement. He was operated on the day after admission, under spinal anesthesia, and an abscess of the left lower quadrant was drained. The following morning temperature was 105°, pulse 130, respirations 36. Cyanosis was present, and râles were heard at both bases. In the afternoon the temperature was 105.6°, pulse 132, respirations 36. The pulse gradually became weaker, the cyanosis increased, and he died that evening.

CASE XXVIII.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 570 grams. There were mural thrombi in the left ventricle and right auricle, and an infarct of the lower lobe of the right lung, as well as multiple infarcts of the spleen, and old infarcts of the kidneys.

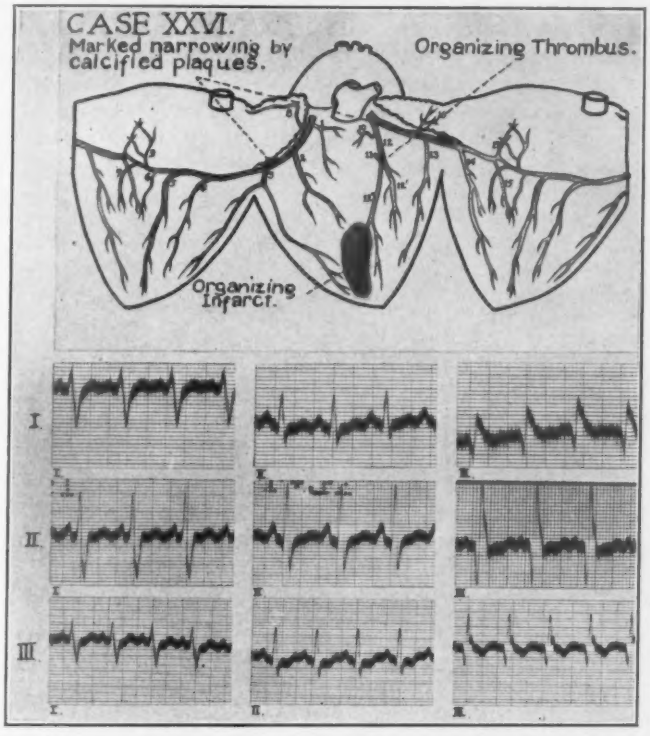

Fig. 27.—Case XXVI. Electrocardiogram No. 1 taken about eighty-four hours after onset of clinical attack. Electrocardiogram No. 2 taken five and one-half days after onset. Electrocardiogram No. 3 taken twelve and one-helf days after onset.

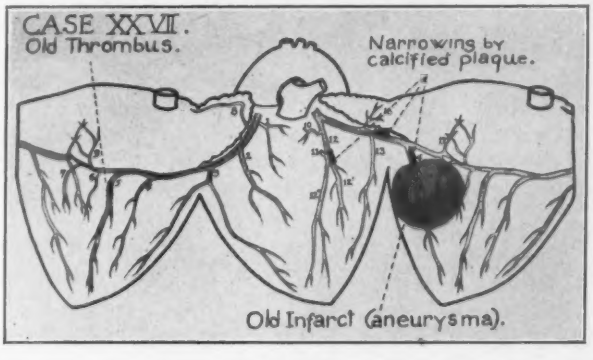

Fig. 28.

Clinical Findings: Male, aged fifty-eight years. Two and one-half years previously he had had an attack of squeezing pressure under the sternum associated with pain in the left forearm from shoulder to elbow. The attack lasted about ten hours and was accompanied by a fall of 30 mm. in systolic blood pressure. Following his

recovery there was occasional substernal pressure sense on exertion. About one year later there was a second severe attack of substernal pressure pain, not radiating to the arm but accompanied by vertigo, unconsciousness, cold, clammy sweat, and pallor. There was no fever or vomiting. He was in bed four weeks and was confined to the house two weeks. Following the second attack, dyspnea, weakness, and loss of weight were prominent symptoms. He was admitted to the hospital because of these. Physical findings were those of enlarged heart with possible left pleural effusion. Blood pressure was 112/68. He was readmitted (one and one-half months later) because of orthopnea, dyspnea, and insomnia. There was bilateral pleural effusion. Some slight substernal distress was present, but no anginal attacks. Blood pressure was 110/88. He was readmitted, ten months later, because of advanced congestive heart failure of two days' duration. He had been more or less in failure since the previous discharge. There was no precordial pain. Blood pressure was 140/88. Temperature was 101.2°, pulse 108, respirations 36 to 50. Twenty-four hours after admission, while lying fairly quietly in bed, he suddenly slumped forward, became more cyanotic and died. Diagnosis: Generalized arteriosclerosis;

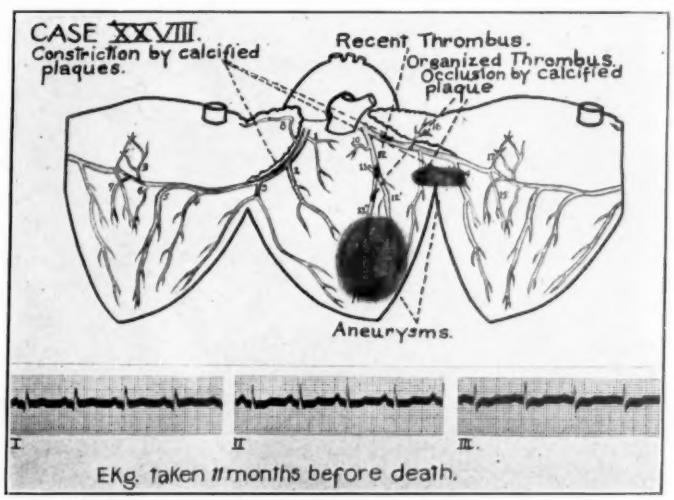

Fig. 29.

coronary sclerosis; cardiac hypertrophy and dilatation; recent coronary thrombus; congestive heart failure; possible pulmonary embolism.

Electrocardiogram: The record was taken on first admission, about two and one-half years after second severe attack. It shows sinus rhythm, occasional ventricular extrasystoles (not shown in illustration).

CASE XXIX.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 600 grams. Mural thrombi were present in the right auricle and multiple infarcts in the lower lobes of both lungs. There was also a marked glandular hyperplasia of the prostate. An old healed apical tuberculosis was found in both lungs and a recent encephalomalacia in the left parietal lobe.

Clinical Findings: Male, aged fifty-nine years. There had been one attack of angina pectoris about two years previously, one six months previously, and several attacks since. Hypertension had been present for some time. On admission, he had pain in the precordial area, radiating to the medial side of the left arm, the right clavicle and the right side of the neck. Blood pressure on admission was 136/106-

112/90, on the third day 118/88, on the fifth day 132/102, and on the seventh day 112/90. White blood count was 11,750. Temperature on admission was normal, rising to 100.2°. There was evidence of pulmonary and cerebral emboli. While in the hospital he had frequent attacks of weakness and cyanosis, and on the fourteenth day, after an attack of severe pain in the right arm, he died suddenly. Diagnosis: Coronary sclerosis; coronary occlusion old and recent; myocardial infarction.

Electrocardiograms: The first record shows sinus rhythm; intraventricular block; ventricular ectopic impulses. The second and third records are essentially similar.

CASE XXX.—Myocardial infarction, "sudden" death.

Autopsy Findings: The heart weighed 475 grams. Mural thrombi were present

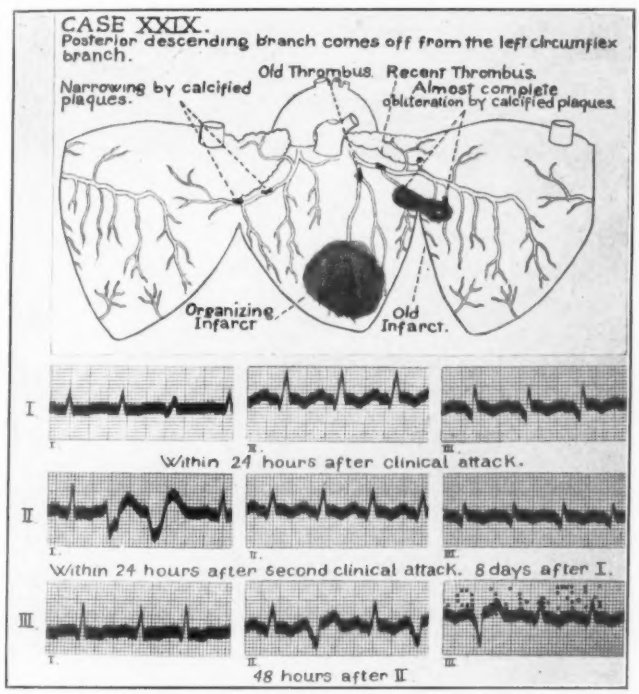

Fig. 30.

in the left ventricle and right auricle, and several emboli were found in the pulmonary arteries. There was a bilateral healed fibrous pleuritis.

Clinical Findings: Female, aged sixty years. Complaints: Recurring attacks of pain in the face and a choking sensation in the region of the episternal notch, for five months. The attacks lasted from a few hours to a day. There was no radiation into the arm. Weakness, dyspnea, substernal pain shifting to the precordial area were associated symptoms and persisted up to the time of admission. Physical Findings: Generalized arteriosclerosis, faint, distant heart tones, blood pressure 130/104, temperature 98.6°, later rising to 101.8°, white blood count 15,400. Twenty-two days after admission she died suddenly while being moved to another bed. Diagnosis: Coronary occlusion.

Electrocardiograms: The records show sinus rhythm, intraventricular block, indeterminate type.

CASE XXXI.—Coronary thrombosis, "sudden" death.

Autopsy Findings: The heart weighed 425 grams. There was also an organizing bronchopneumonia, with abscess formation in the right lower lobe, and an old healed tuberculosis in the upper portions of the right upper lobe.

Clinical Findings: Male, aged seventy-three years. He was admitted because of diabetes and progressive weakness of the legs, leading to a fall the day before admission. Diabetes had been present for ten or twelve years, the weakness for three or four months. There was no cardiac pain. Physical Findings: Pulse 100, temperature 98.2°, white blood count 18,000, blood sugar 312, acetonuria. Six days before death (two days after admission) he felt pain in the chest, particularly on coughing, and auricular fibrillation developed. Later there was a right pleural effusion, temperature 101°, pulse 120. The auricular fibrillation stopped. Four days after admission the patient suddenly became cyanotic, restless, had labored breathing,

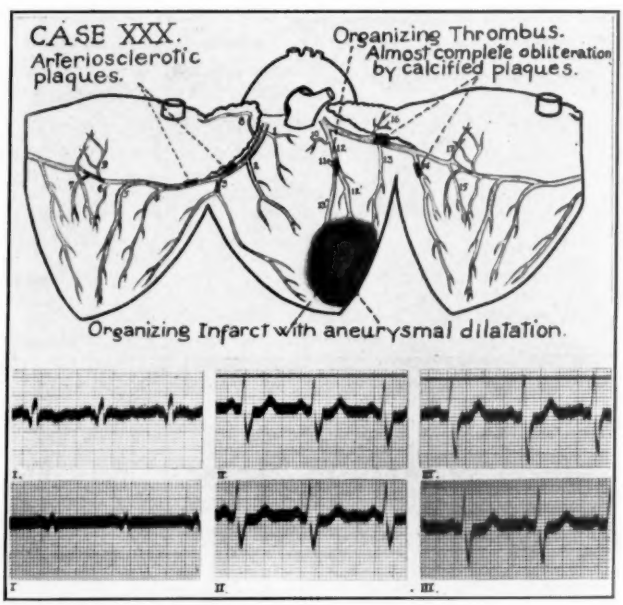

Fig. 31.—Case XXX. Electrocardiogram No. 1 taken approximately five months after clinical attack. Electrocardiogram No. 2 taken two days later (twenty days before death).

and died. No blood pressure was taken. Diagnosis: Diabetes mellitus; coronary sclerosis; probable coronary occlusion.

CASE XXXII.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 400 grams. There were also an acute diverticulitis and a circumscribed peritonitis. A large stone was present in the gallbladder. The left leg had been amputated at the midportion of the thigh.

Clinical Findings: Male, aged fifty-six years. Complaint: Soreness over the left inguinal region, accompanied by a sharp shooting pain in the lower abdomen, radiating upward to the level of the umbilicus; nausea and vomiting. There were no cardiac symptoms at the time of admission or previously. Physical Findings: Temperature 103.2°, pulse 80, respirations 80, blood pressure 140/90; white blood count was 11,400. The heart was slightly enlarged to the left; tones were somewhat distant, but regular. The abdominal signs were those of acute peritonitis,

probably localized in the left lower quadrant. Diagnosis: Acute peritonitis. Under ethylene anesthesia laparotomy was done immediately. Free pus and an acute inflammatory mass at the rectosigmoid junction were found. The mass was drained, and a colostomy was performed. The patient left the operating table in critical condition. The next day, the temperature rose to 105.2°, pulse 126. On the third day, temperature was 106.2°, pulse 124, respirations 64 and shallow. The pulse gradually grew weaker, and the patient died on the third day after operation.

CASE XXXIII.—Coronary thrombosis, "sudden" death.
Autopsy Findings: The heart weighed 425 grams.

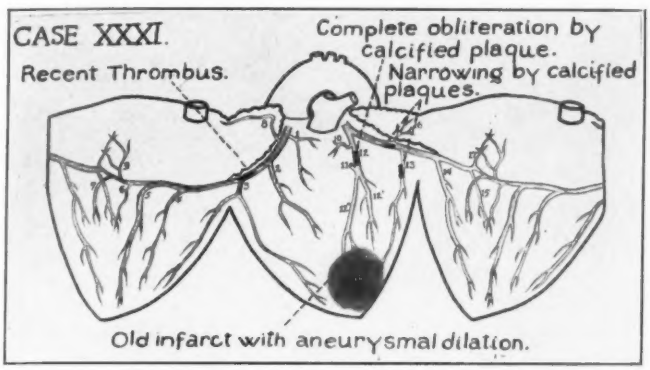

Fig. 32.

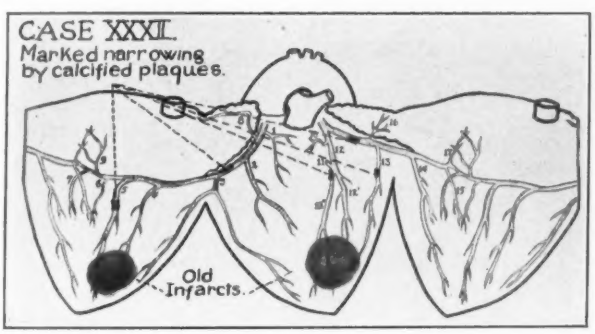

Fig. 33.

Clinical Findings: Female, aged sixty-eight years. She was admitted because of gangrene of the right toe of three weeks' duration. Diabetes mellitus had been present for eight years. There were no cardiac symptoms at any time. Physical Findings: Generalized arteriosclerosis, temperature 100.6°, pulse 100, respirations 22, white blood count 14,500, blood pressure 178/92, blood sugar 348, N.P.N. 32. The first heart sound was muffled, otherwise nothing abnormal was noted. Diagnosis: Diabetes mellitus; gangrene of toe; arteriosclerotic heart disease. Attempts to clear up the gangrene with diet and insulin failed. There were two occasions of insulin shock. Under spinal anesthesia amputation was performed twenty-one days after admission. She was found dead in bed on the fifth postoperative day. During the operation, the blood pressure dropped to 102/60; it was 128/60 at the end of operation.

CASE XXXIV.—Myocardial infarction, "gradual" death.

Autopsy Findings: The heart weighed 425 grams. Pulmonary emboli and a small infarct in the right lung were also found.

Clinical Findings: Male, aged sixty-eight years. Arteriosclerotic hypertensive heart disease with auricular fibrillation had been present for four or five years. For a time auricular fibrillation was controlled by quinidine. In the spring of 1930

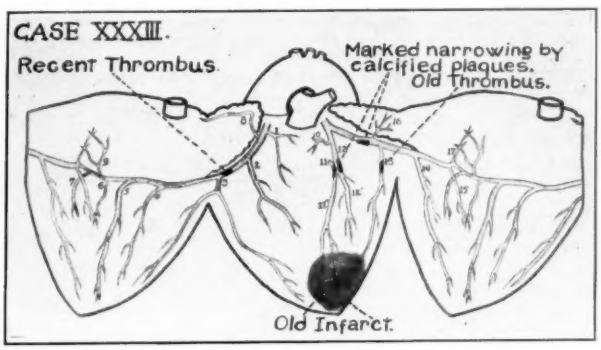

Fig. 34.

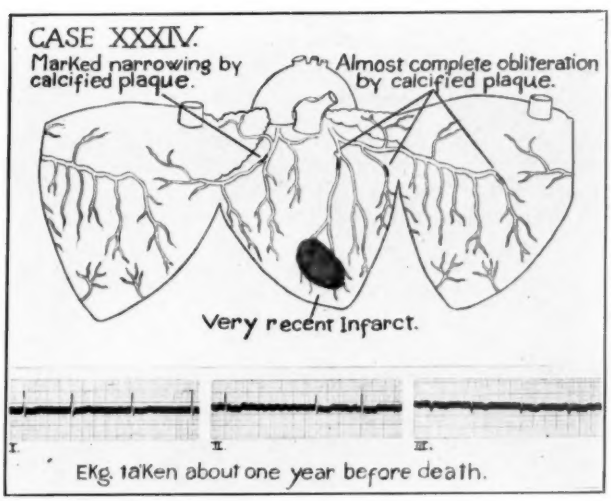

Fig. 35.

he suffered an acute heart attack which was thought by his physician to be a coronary occlusion. A few months later, following exertion, he felt a sudden severe pain in the right chest associated with weakness and dyspnea. Again he was thought to have a coronary occlusion and, possibly, an infarct of the right lung. He made a fairly satisfactory recovery from this attack but never regained his previous state of health, having from time to time periods of Cheyne-Stokes breathing, confused mental states, suppression of urine, pain in the small joints of his hands and feet, associated with low grade fever. Death occurred in the fall of 1931. About a week previous to death, after an unusually strenuous business day

and after dinner, he complained of dizziness and faintness associated with numbness and weakness of his left arm. The following night there was an attack of severe chest pain in the region of the right nipple, unrelieved by morphine, followed by nausea, vomiting, fever, and hemoptysis. Diagnosis: Coronary thrombosis.

Electrocardiograms: The record taken September, 1928, shows sinus rhythm; right axis deviation; low amplitude in the second and third leads. The record taken October, 1930, shows slow auricular fibrillation. The record taken in 1931, three weeks before death, shows inversion of T-wave in Leads II and III. (Only the 1930 record is reproduced.)

(To be continued.)

TREATMENT OF ANGINA PECTORIS AND CONGESTIVE FAILURE BY TOTAL ABLATION OF THE NORMAL THYROID*†

XIV. Results in Arteriosclerotic Heart Disease

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SINCE the course of cardiovascular disease varies according to its etiological basis, it has seemed worth while to analyze our results in the treatment of various types of chronic heart disease by total ablation of the thyroid so that the value of the procedure may become more clearly established for each type. Seventy-five patients with chronic cardiovascular disease have been treated by total thyroidectomy at the Beth Israel Hospital during the past eighteen months.[1, 2, 3, 4] Thirty-six patients were diagnosed as having arteriosclerotic heart disease. This communication is a summary of our results in treating this group. Before operation these patients, despite the use of all available medical procedures, were incapacitated because of attacks of angina pectoris, cardiac asthma, congestive failure, paroxysmal heart action, or combinations of these conditions. The ages ranged from forty-two to seventy years; twenty-six patients were fifty-five years of age or over. Fifteen had hypertension, and in fourteen there was a history of coronary occlusion (Tables I and II).

RESULTS

Angina Pectoris.—Of 36 patients suffering from the various forms of arteriosclerotic heart disease, 31 had definite angina pectoris (Table III). Of this number 12 are now able to perform work which had been impossible for months to years before operation; 7 of these 12 have been completely free of attacks for three to eighteen months after operation and have never required nitroglycerine. The average duration of complete relief is eleven months. Another group of 5 patients were completely relieved for three to nine months but have had recurrence of pain. Three patients have been completely free of pain but are limited in activity by myocardial failure. Of the remaining 11 patients, 5 have attacks which are less severe and less frequent. Since these patients still experience frequent attacks and are unable to perform work, we

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TABLE I

RESULTS IN THIRTY-SIX PATIENTS WITH ARTERIOSCLEROTIC HEART DISEASE

SERIAL NUMBER	AGE	SEX	BLOOD PRESSURE	ATTACK OF CORONARY OCCLUSION BEFORE OPERATION	DURATION OF SYMPTOMS BEFORE OPERATION			CONDITION BEFORE OPERATION AND AT PRESENT TIME	
					ANGINA PECTORIS	CARDIAC ASTHMA	CONGESTIVE FAILURE		
1	52	M	130/ 80	3½ yr.	3 yr.		3 yr.	Before:	Confined to bed—chronic hospital—three years.
								18 mo. after:	Laboratory assistant 14 mo.—8 hr. daily. Symptom free.
5	55	M	188/ 90		2 yr.	2 yr.	2 yr.	Before:	Confined to bed in chronic hospital.
								15 mo. after:	Up and about all day. Symptom free.
7	57	M	140/ 84		18 mo.			Before:	Angina on exertion, unable to work for one year.
								15 mo. after:	Day laborer, heavy work, 11 mo. Symptom free.
8	57	M	120/ 96		1 mo.	2 mo.	2 mo.	Before:	Bronchiectasis.
								1 day after:	Died 1 day after operation.
10	60	M	190/110			2 yr.	1 wk.	Before:	Unable to work over a year, confined to bed for 7 wk.
								3 wk. after:	Definite improvement, 3 wk. Attack of pulmonary edema and died.
14	53	M	120/ 80		1 yr.	1 yr.	1 yr.	Before:	Unable to work, confined to bed for 4 mo.
								12 mo. after:	Furniture salesman, 10 hr. daily, past 8 mo. Symptom free.
15	59	F	150/ 90		7 mo.			Before:	Daily attacks of angina at complete bed rest for 7 mo.
								12 mo. after:	Doing part of housework, 9 mo. Slight attack on exertion every 2-3 wk.
16	49	M	160/110	5 yr. 2 yr.	6 yr.			Before:	Unable to work for 2 yr. Frequent, prolonged, severe attacks of angina.
								12 mo. after:	Attacks less frequent and less severe.
17	58	F	146/ 86		15 yr.			Before:	Frequent severe angina on exertion, at rest, and during sleep.
								12 mo. after:	Working part time. Attacks less frequent, less severe, never during sleep.

TABLE I—CONT'D

SERIAL NUMBER	AGE	SEX	BLOOD PRESSURE	ATTACK OF CORONARY OCCLUSION BEFORE OPERATION	DURATION OF SYMPTOMS BEFORE OPERATION				CONDITION BEFORE OPERATION AND AT PRESENT TIME
					ANGINA PECTORIS	CARDIAC ASTHMA	CONGESTIVE FAILURE		
18	63	M	135/ 90		9 mo.	9 mo.	5 yr.	Before:	Renal insufficiency and intractable edema.
								1 day after:	Died 1 day after operation.
19	63	M	125/ 60		7 yr.	2 yr.	5 yr.	Before:	Intractable edema.
								11 mo. after:	Better but activity limited.
20	57	M	110/ 65	2 yr. 1½ yr.	2 yr.			Before:	Frequent severe, prolonged attacks of angina even at rest.
								11 mo. after:	Attacks less frequent, less severe, none at rest.
21	54	M	130/ 80	6 yr.	6 yr.			Before:	Unable to work because of severe angina.
								11 mo. after:	Worked full time without pain 2nd to 9th mo. Angina recurred 9 mo. after operation following automobile accident.
22	59	M	130/ 80				2 yr.	Before:	7 hospital admissions in 2 yr., bedridden almost constantly.
								11 mo. after:	Working full time, past 6½ mo. Symptom free.
25	65	M	120/ 80		2½ yr.			Before:	6 mo. partially bedridden, frequent attacks of angina pectoris.
								11 mo. after:	Working as salesman, past 8 mo. Attacks very rare, only on severe exertion in cold.
26	55	M	120/ 80				18 mo.	Before:	Bronchiectasis.
								1 day after:	Died 1 day after operation.
33	57	F	210/120		2 yr.			Before:	Unable to do housework. Frequent attacks of angina and palpitation.
								9 mo. after:	Doing all housework, 6 mo. Symptom free.
37	63	M	170/110	3 yr.	3 yr.	2 mo.	2 mo.	Before:	Intractable edema and hydrothorax.
								7 mo. after:	Activity limited. Congestive failure readily controlled, rare attacks of cardiac asthma, no angina.

TABLE 1—CONT'D

SERIAL NUMBER	AGE	SEX	BLOOD PRESSURE	ATTACK OF CORONARY OCCLUSION BEFORE OPERATION	DURATION OF SYMPTOMS BEFORE OPERATION				CONDITION BEFORE OPERATION AND AT PRESENT TIME
					ANGINA PECTORIS	CARDIAC ASTHMA	CONGESTIVE FAILURE		
40	62	F	170/ 90					Before:	Frequent attacks, paroxysmal auricular tachycardia —6½ yr.
								7 mo. after:	Attacks less frequent.
41	49	M	160/100	6½ yr.	6½ yr.	11 mo.		Before:	Confined to bed 5 mo. Attacks on rest, exertion, excitement, during sleep.
								7 mo. after:	Working as executive. Rare attacks on overwork.
42	64	M	145/ 70	1 yr.	20 mo.			Before:	Daily attacks although working as painter.
								7 mo. after:	Working full time, 4 mo. Symptom free. Coronary occlusion and return of attacks four months after operation.
45	44	M	145/ 85		4 yr.			Before:	Frequent attacks daily of angina pectoris.
								7 mo. after:	Working. Rare attacks on exertion.
46	60	M	155/100	4 yr.	4 yr. 9 mo.		3 mo.	Before:	Confined to bed for 10 wk.
								7 mo. after:	Activity limited, angina less frequent, no congestive failure.
47	52	M	120/ 70	16 yr.	16 yr. 18 mo.			Before:	Frequent, prolonged and intractable attacks of angina.
								6 mo. after:	Attacks less severe and less frequent.
50	54	M	180/110		10 yr.			Before:	Unable to work for 6 mo.
								4 mo. after:	Able to work 3 mo. after operation. Attacks recurred only with excessive thyroid medication.
51	53	M	140/ 80		6 yr.			Before:	Activity limited 6 yr. Unable to work for 2 mo.
								5 mo. after:	Able to work 4 mo. Attacks recurred with excessive thyroid medication.
57	70	F	170/105	3 mo.	7 yr.	6 mo.		Before:	Bed and chair 1 yr. Confined to bed for 3 mo.
								3 mo. after:	Moderate activity. Symptom free 3 mo. Died of coronary occlusion.

TABLE I—CONT'D

SERIAL NUMBER	AGE	SEX	BLOOD PRESSURE	ATTACK OF CORONARY OCCLUSION BEFORE OPERATION	DURATION OF SYMPTOMS BEFORE OPERATION			CONDITION BEFORE OPERATION AND AT PRESENT TIME	
					ANGINA PECTORIS	CARDIAC ASTHMA	CONGESTIVE FAILURE		
59	58	F	180/100	8 mo.	11 mo.			Before:	Confined to bed for 6 mo.
								4 mo. after:	Moderate activity. Attacks recur only with excessive thyroid.
60	42	M	180/110		20 mo.			Before:	Unable to work for 4 mo.
								2 mo. after:	Completely free from attacks and able to work.
61	58	F	180/100				5 yr.	Before:	Intractable edema and hydrothorax at complete bed rest.
								4 mo. after:	Returned to full household duties 1 mo. after operation. Slight recurrence of edema. Now improved.
64	62	M	170/ 80		5 mo.			Before:	Daily attacks of angina on exertion, rest and during sleep.
								3 mo. after:	Free from attacks and working as an executive.
65	65	M	130/ 70	3 yr.	9 yr.	3 mo.	1 yr.	Before:	In bed the greater part of 3 yr.
								2 mo. after:	Up and about 2 mo., attacks less severe and less frequent.
67	58	M	150/ 96		5 yr.	1½ yr.	4 mo.	Before:	Confined to bed for 1 yr.
								2 mo. after:	Symptom free since operation.
69	65	F	130/ 70		2 mo.	6 mo.		Before:	Confined to bed for 6 mo.
								1 mo. after:	Symptom free since operation.
70	57	M	135/ 80	1 mo.	3 yr.	1 yr.	1 yr.	Before:	Confined to bed for 5 mo.
								1 mo. after:	Symptom free since operation.
71	57	F	150/ 90	6 mo.	4 yr.			Before:	Unable to do housework for 1 yr.
								1 mo. after:	Symptom free since operation.

TABLE II

SYMPTOMATOLOGY IN 36 PATIENTS WITH ARTERIOSCLEROTIC HEART DISEASE

Angina pectoris only	17
Congestive failure only	3
Cardiac asthma only	0
Paroxysmal auricular tachycardia	1
Angina and cardiac asthma	4
Angina and congestive failure	2
Congestive failure and cardiac asthma	1
Congestive failure, cardiac asthma and angina pectoris	8

do not feel that they have been materially benefited. Three patients are recently postoperative. Three patients who were operated on primarily for congestive failure or cardiac asthma died postoperatively. One of these patients, a woman seventy years old, died after three months of complete relief.

TABLE III

RESULTS IN 31 PATIENTS WITH ANGINA PECTORIS

Now working (average 10½ months)		12
Completely free of attacks	7	
Recurrence of angina after 3-9 months of complete relief*		5
Free of angina but activity limited		3
Attacks less severe and less frequent		5
Recently postoperative		3
Postoperative deaths†		3

*One of these patients died of coronary occlusion after three months of complete freedom from angina.

†All postoperative deaths occurred in patients with advanced congestive failure.

Cardiac Asthma.—Thirteen patients with cardiac asthma experienced attacks at least several times a week for months to years prior to operation (Table IV). Three of these patients are still entirely free from

TABLE IV

RESULTS IN 13 PATIENTS WITH CARDIAC ASTHMA

Entirely free from attacks		3
Working	2	
Attacks less frequent		2
Recently postoperative		4
Deaths*		4

*Three of these patients had advanced congestive failure. The fourth died of coronary occlusion after three months of complete freedom from attacks.

attacks, seven, twelve, and fifteen months after operation. Two of these have returned to work. Two patients who had frequent attacks prior to operation are greatly relieved, in that the attacks are far less frequent. Less than two months have elapsed since operation in four patients, and, although the patients have not been permitted to be up and about, they are free of attacks for the first time in many months. Four patients, including the three patients with angina pectoris previously mentioned, died postoperatively. One of these patients was free of attacks for three months.

Congestive Failure.—Of fourteen patients with congestive failure (Table V), five have maintained compensation for seven to eighteen

months, during which time they have been enjoying activity which was impossible for one to three years. The average postoperative duration is thirteen months. Three, previously bedridden and destitute, have been

TABLE V

RESULTS IN 14 PATIENTS WITH CONGESTIVE FAILURE

No return of congestive failure 7-18 mo. (average 13 mo.)		5
Working	3	
Recurrence of congestive failure on activity		3
Recently postoperative		2
Deaths		4

working from eight to ten hours daily, seven, eight, and fourteen months, respectively. Three patients, decompensated and bedridden for one-half to two and a half years, have shown moderate improvement but have been unable to assume activity without redeveloping decompensation. The reasons for this lack of greater improvement will be discussed later. Two patients are recently postoperative. Four patients, previously mentioned in the discussion of angina pectoris and cardiac asthma, died postoperatively.

Paroxysmal Heart Action.—Our experience in the treatment of paroxysmal heart action is too limited to allow any conclusions to be drawn. One patient with paroxysmal auricular tachycardia of arteriosclerotic origin has had fewer and less severe attacks since operation. Another patient with paroxysmal auricular fibrillation of rheumatic origin has been completely free of attacks for six months since operation.

COMMENT

The life expectancy of patients with arteriosclerotic heart disease is limited necessarily by their advanced age. Total ablation of the thyroid gland, however, offers an opportunity to increase the years of useful work and happiness in such patients. The results in paroxysmal nocturnal dyspnea are especially noteworthy, for medical therapy can do little to relieve or prevent the progress of this condition.[5, 6, 7]

In spite of advanced years and poor physical condition, patients with arteriosclerotic heart disease withstand the operation well. The presence of renal impairment, chronic pulmonary infection, or intractable edema, however, increases the operative risk tremendously and makes a life of activity and comfort improbable. We feel, therefore, that the operation should not be performed in such patients.

The therapeutic benefits of total ablation of the thyroid parallel the lowering of the basal metabolism. As has been pointed out elsewhere,[4, 8, 9] the untoward symptoms of myxedema frequently become evident when the basal metabolism falls to approximately minus 30 per cent. These symptoms can be readily alleviated with small doses of thyroid without materially detracting from the benefits obtained by lowering the basal metabolism. In our experience, the basal metabolic

rate is frequently low in apparently normal individuals,[10] and especially in patients suffering from angina pectoris.[10, 11] In such patients little improvement can be expected from the operation, for thyroid medication will be required before an appreciable drop in basal metabolic rate has been obtained.

The results in the fifteen patients with high blood pressure demonstrate that the presence of hypertension does not contraindicate the procedure. There were no postoperative deaths in this group, and five of the thirteen patients have been able to work and maintain their improvement. In no instance was the blood pressure lowered by the operation to any appreciable extent.

It is of interest to examine the course of patients who gave a previous history of coronary thrombosis (Table VI). Fourteen of our patients

TABLE VI

RESULTS IN 14 PATIENTS WITH HISTORY OF PREVIOUS CORONARY OCCLUSION

Working	2
Temporary improvement	6
No improvement*	4
Recently postoperative	2

*In these patients the preoperative basal metabolic rates ranged from minus 14 to minus 24 per cent.

suffered one or more attacks prior to operation. In four of this group, improvement was hardly to be expected because of lowered preoperative basal metabolic rates. Of the remaining 10, 2 patients have shown decided improvement, 2 are recently postoperative, while the remaining six showed definite but only temporary improvement. These results again seem to indicate that coronary occlusion is usually evidence of severe, generalized, progressive coronary sclerosis. In some patients who have done well, coronary thrombosis may have been due to localized coronary disease, the remaining vasculature being relatively normal. Since one cannot differentiate between these two groups, the effects of operation in patients with healed coronary thrombosis cannot be prognosticated with confidence.

The above considerations suggest that the presence of certain signs and symptoms militate against the benefits which may be derived from this procedure. If these are borne in mind, patients in the future may be more carefully selected, and the incidence of poor or fair results decreased. The fact that eighteen of the total thirty-six patients operated upon showed no such unfavorable factors and have shown striking clinical improvement which has been maintained to date affords a strong basis for this opinion. This view is also supported by the fact that 63 per cent of patients with rheumatic heart disease and congestive failure have been able to return to work.[12] In patients with rheumatic heart disease, coronary occlusion is rare; the patients are usually relatively young; and the basal metabolic rate is rarely low. The value of the procedure in the treatment of patients with arteriosclerotic heart disease is

demonstrated by the fact that ten patients who would otherwise be forced to spend the greater part of their lives in bed have been enabled to return to remunerative occupations or housework, while ten more are able to work part time or would be capable of working if suitable occupations could be found (Table VII). The final evaluation of the

TABLE VII

SUMMARY OF RESULTS IN 36 PATIENTS WITH ARTERIOSCLEROTIC HEART DISEASE

Working full time	10
Working part time or able to work	10
Unable to work	6
Recently postoperative	5
Postoperative deaths*	3
Subsequent deaths	2

*All deaths occurred in patients with advanced congestive failure.

therapeutic results of total ablation of the thyroid awaits observations over an extended period of years. The results to date, however, are sufficiently favorable to warrant the belief that this procedure deserves a place in the treatment of arteriosclerotic heart disease.*

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*During the year that has elapsed since the presentation of the above data, there have been some variations in the clinical conditions of the patients. In general, however, clinical improvement has been maintained.

THE EFFECT OF POSITION OF THE HEART ON THE ELECTROCARDIOGRAM

I. The Electrocardiogram in Revived Perfused Human Hearts in Normal Position*

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ALL the original experimental work on the electrocardiogram was necessarily made on lower animals.[1, 2, 3] Of those used, the dog was most extensively studied. The results of such investigations were for many years the basis of interpretation of human electrocardiology, especially in localization of ventricular extrasystoles, bundle-branch block and ventricular preponderance. A great deal of this experimental work was done by Thomas Lewis[4] and his coworkers, whose studies formed the basis of the conventional interpretation of the electrocardiogram. That interpretation was first challenged in 1920 by Oppenheimer and Pardee[5] as a result of anatomical studies, and by Farr[6] from theoretical conclusions. Little attention was paid to these exceptions until Barker, Macleod and Alexander[7] stimulated directly the human heart in a case of purulent pericarditis. They found that what had been considered a right ventricular extrasystole was in reality a left ventricular extrasystole, and conversely, a left ventricular extrasystole was in reality a right. Such reversal of extrasystoles applied only to those having a discordant type of curve, whereas no differences were found in those having concordant types. On theoretical grounds these authors assumed that what had been considered a right bundle-branch block in the conventional interpretation of electrocardiograms was in reality a left bundle-branch block, and a left bundle-branch block was therefore a right. In two other cases, the left ventricle of the human heart has been directly stimulated, and the results have been essentially the same as those of Barker and his coworkers.[8, 9] In both of these cases a purulent pericarditis was also present.

There have been five other attempts[10-14] to interpret electrocardiograms by studying the human heart. The results of these experiments cannot be considered reliable because in most instances the heart was not exposed, and therefore there is much uncertainty as to which ventricle was stimulated.

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The subject has been studied further by Katz and his coworkers,[15] whose results and conclusions served to confuse the subject rather than to clarify it. They showed not only that extrasystoles could be reversed by changing the position of the heart, but also that bundle-branch block could be likewise reversed by the same means, both under experimental conditions in the dog and also in man by changing the position of the body. They stated that there was no proof that the human hearts which were directly stimulated were in normal position, and they believed that conclusions drawn from such experiments could not be considered trustworthy. They further claimed that localization of bundle-branch block and extrasystoles in man was impossible.

Many attempts have been made to solve the problem by post-mortem examination of human hearts in which bundle-branch block had been present before death. The results of these studies have failed to clarify the subject. Eighteen attempts to find the lesion histologically in cases of bundle-branch block are recorded. In many cases lesions were found which apparently agreed with the conventional electrocardiogram.[16-20] On the other hand, lesions in the opposite bundle were noted by Oppenheimer and Pardee[5] and by Wolferth, Margolies and Bellet.[21]

The results of anatomical studies are further complicated by a fact that is well known, that bundle-branch block may be functional rather than organic and therefore may have no pathological significance. Cohn and Lewis[22] were unable to detect any lesions in either bundle in the hearts of patients who had had bundle-branch block.

In view of the uncertainty of the results obtained both from an experimental and from a pathological approach to the subject, it is obvious that other methods of investigation must be sought. Cutting the bundle in the heart of man and studying the resulting change on the electrocardiogram in the revived perfused heart has never been done until the present time, and is the most direct method by which one may establish the true nature of the lesion.

The effect of changing the position of the human heart has never been studied directly. Notation has been made of changes in axis deviation after shifting the patient in various positions,[23] and, also, of the variations that take place following shift of the mediastinum after such procedures as pneumothorax and thoracoplasty. Treiger and Lundy[24] have recently studied the change in the electrical axis after pneumothorax in forty-one cases. They found that both left and right pneumothorax caused a shift of the electrical axis to the right when there were no adhesions or fluid in the pleural cavity. These complications, however, could cause a shift of the axis to the left.

Nathanson[23] studied the effect of change of position on the electrocardiogram in sixty individuals by taking tracings from the patients in the reclining and in the left and right lateral positions. In five

cases no change was noted, while in the remaining fifty-five most of the tracings taken in the left lateral position changed in the direction of a right ventricular preponderance, although some became more of a left. In the right lateral position there was no variation in 30 per cent of the cases, while the remaining 70 per cent were divided equally between right and left preponderance. In such a study it is impossible to tell the degree of rotation of the heart on its long axis, and since rotation has a profound effect on the electrocardiogram, the tracings obtained cannot be considered as indicating the result of the shift of the heart alone. In view of the marked difference between the electrocardiogram of the dog and that of man, the curves obtained by changing the position of the dog's heart do not necessarily reflect what occurs in man. In the latter instance, to obtain accurate data of the effect of axis deviation on the electrocardiogram it would be essential that the human heart be shifted under conditions in which its exact position is known, a procedure which never has been done heretofore.

We have recently shown that in the presence of pericarditis in the dog, an inversion of the usual extrasystoles found by Lewis in the dog were obtained. In view of the fact that all three human cases, in which direct stimulation of the human heart was done, had a purulent pericarditis, it was felt that it was necessary to study the human heart in which the pericardium was normal.

METHOD

Immediately after death, the chest was opened by means of a routine autopsy incision. The pericardium was incised, care being taken to keep the heart in normal position. The heart was then perfused with whole blood by a modification of the method described by Langsdorf. A cannula was inserted into the aorta, through which blood was introduced at a pressure of 120 mm. of mercury. It was always necessary to take precaution against permitting air to enter the coronary arteries. In most cases the cardiac nerves were cut. In a properly made preparation the auricles usually began to fibrillate or beat, followed by fibrillation of the ventricles. Usually with an increase in the coronary artery pressure, runs of ventricular extrasystoles developed with final slowing of the heart to a normal rhythm. In some instances nodal or ventricular foci became the pacemaker for the heart. Electrocardiograms were obtained by using the standard leads of the body.

In a total of thirty-seven cases studied by this method eight gave normal appearing electrocardiograms. The majority of the others gave curves which showed variations, such as inverted T-wave in Lead I, prolongation of the P-R interval, and the QRS complex. The atypical curves resulted from many factors, some of which could be corrected in the preparation. Chief among the causes of atypical appearing curves

were low temperature of the perfusing solution, freshness of the perfusing blood, delay in obtaining the body, or changes that occurred in the heart before death. Pathological hearts usually have more extreme changes than normal ones. Under as nearly ideal circumstances as is possible to attain, fairly normal appearing electrocardiograms may be obtained.

In the experiments in which records were fairly normal the hearts were used to make further observations on the electrocardiogram. The hearts were maintained in a normal position in the chest and extrasystoles were obtained at the 12 points of Barker. In five cases we were successful in cutting the right and left bundle branch. In one instance,

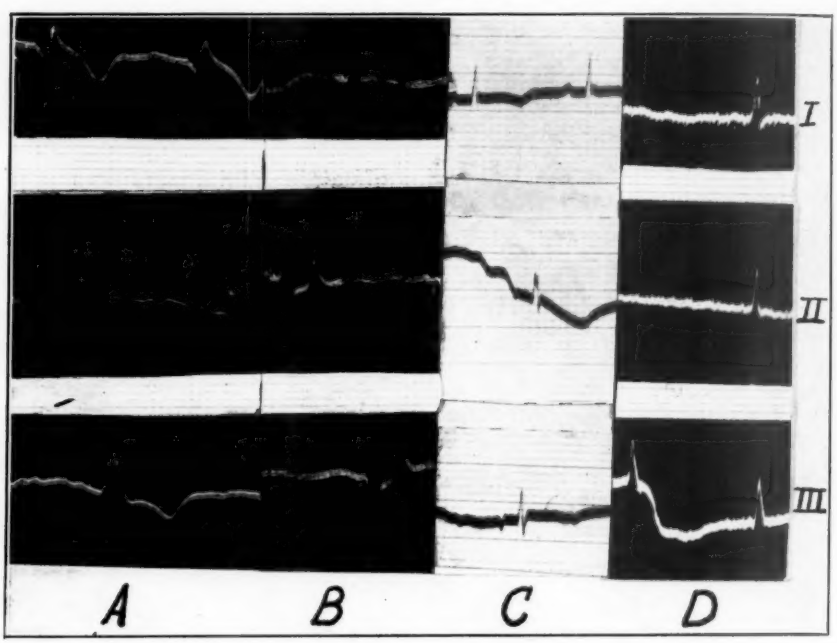

Fig. 1.—Electrocardiograms from four different cases obtained after the hearts were revived. These represent the most normal curves obtained. Minor changes may be noted in the curves such as inverted T-waves, some slurring of the QRS complexes and slightly prolonged conduction time as in Case A. Changes in the mechanism of some of the hearts occur quite rapidly because of the variability of the pacemaker as in Case D.

the effect of changing the position of the heart was studied. The positions used were rotation through the long axis of the body in a clockwise and counter-clockwise manner, and also displacement of the heart from its normal position to the right and to the left. The divergence was noted in degrees.

RESULTS

Section of the right bundle resulted in a curve, which was not uniform in all experiments. The QRS complex was definitely prolonged

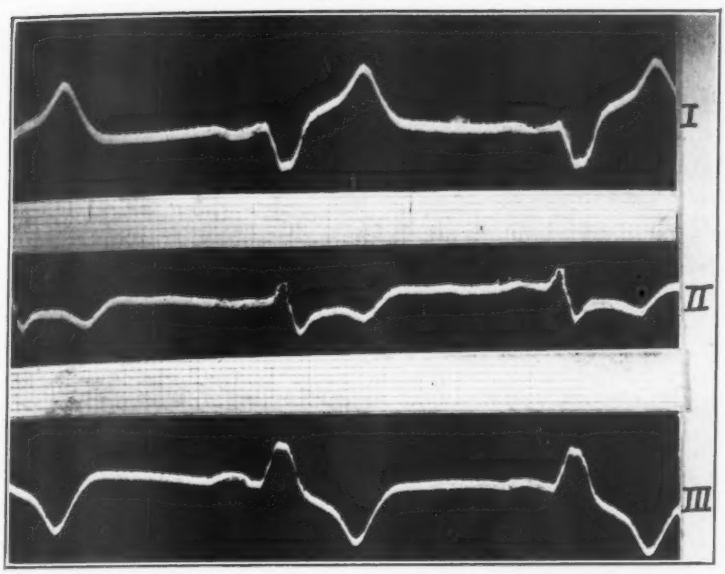

Fig. 2.—Electrocardiographic tracings obtained in a revived perfused human heart after section of the right bundle of the conducting system. It was noted at the time that the left ventricle contracted before the right. Anatomical studies revealed the incision to be along the septum just below the membranous portion.

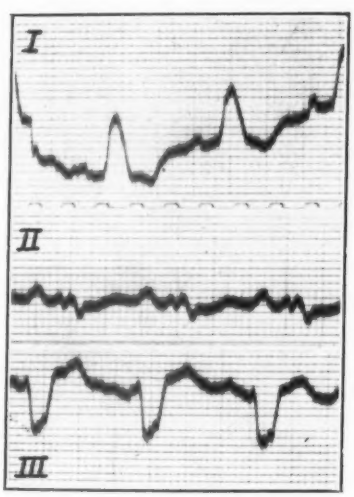

Fig. 3.

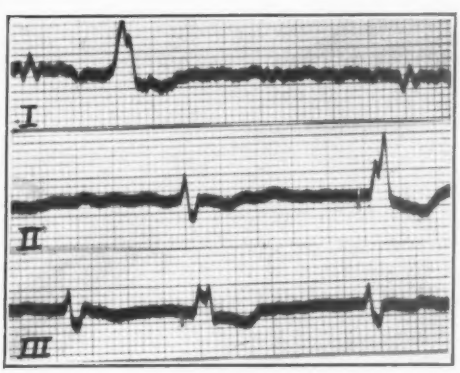

Fig. 4.

Fig. 3.—Electrocardiogram obtained after cutting the left bundle of the revived perfused human heart. Delay in contraction of the left ventricle could be seen after the incision. Anatomical study showed the incision to lie in the septum at the base of the posterior cusp of the aortic valve.

Fig. 4.—Curve obtained by stimulation of the conus of the right ventricle in the region of Point 10, Barker, Leads I, II, and III.

to as much as 0.24 second. The initial deflection was down in Lead I and up in Lead III. In one instance we obtained a rather high deflection in Lead II, followed by inversion of the complex and T-wave. The character of the complex was varied by contact of the ventricle. Atypical curves were sometimes obtained when the heart was in normal position and contact to the body was through the left ventricle only.

When the left bundle was cut with the heart in normal position, curves were obtained in which the initial ventricular deflection was up in Lead I and down in Lead III. The curves were usually inverted in Lead II.

Four general types of extrasystoles were observed. Concordant extrasystoles in which the initial ventricular deflection was upright in all three leads were obtained from stimulation of the conus of the right ventricle.

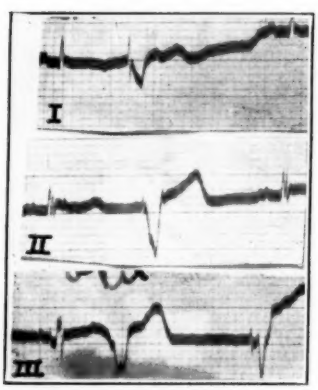

Fig. 5.

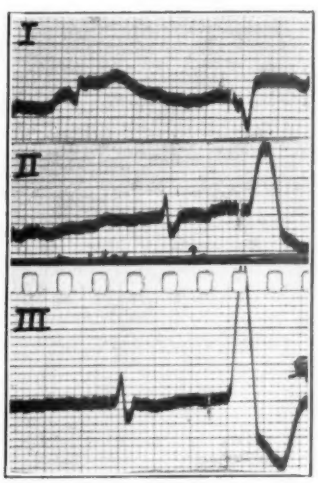

Fig. 6.

Fig. 5.—Discordant curve as obtained on stimulation of the lateral wall of the right ventricle, Point 8, Barker.

Fig. 6.—Extrasystoles obtained on stimulation of the lateral wall of the left ventricle, particularly toward the base of the heart, Point 1, Barker.

Concordant extrasystoles in which the initial ventricular deflection was down in all three leads were obtained from stimulation of the region of the apex of the left ventricle.

Discordant curves in which the initial ventricular deflection was up in Lead I and down in Lead III were obtained by stimulating the right ventricle everywhere except at the conus.

Discordant curves in which the initial ventricular deflection was down in Lead I and up in Lead III were obtained from the left ventricle, except at the apex which covers a relatively greater area posteriorly than it does anteriorly.

The effect of change of position of the heart on the ventricular deflection is summarized in Table I.

TABLE I

EXPERIMENT NO. 35

DEGREE OF DISPLACEMENT OF APEX OF THE HEART	CHARACTER OF COMPLEX					
	LEAD I		LEAD II		LEAD III	
	QRS	T-WAVE	QRS	T-WAVE	QRS	T-WAVE
Normal position 22½° to the left	Upright 7 mm.	Iso-electric	Upright 8 mm.	Inverted 1 mm.	Upright 2 mm.	Inverted 2 mm.
Apex of heart displaced at an angle of 45° to the left	Inverted 4 mm.	Upright 1 mm.	Upright 3 mm.	Iso-electric	Upright 7 mm.	Iso-electric
Apex of heart displaced at an angle of 67° to the right	Upright 8 mm.	Inverted 3 mm.	Upright 2 mm.	Inverted 1 mm.	Inverted 6 mm.	Upright 1 mm.
Heart rotated clockwise	Inverted 3 mm.	Upright 2 mm.	Inverted 2 mm.	Upright 3 mm.	Upright 4 mm.	Inverted 3 mm.
Heart rotated counter-clockwise	Upright 5 mm.	Inverted 3 mm.	Upright 3 mm.	Inverted 2 mm.	Inverted 2 mm.	Upright 2 mm.

The figures which represent the character of the complex are measured in millimeters.

Shift of the heart to the right causes the deflection to be more up (prominent R-wave) in Lead I, with greater inversion in Lead III (prominent S-wave) than normal. This is the curve of left axis deviation. Shift to the left causes lowering or inversion of the QRS complex in Lead I (prominent Q-wave) with a high complex in Lead III (prominent R-wave). Rotation of the heart clockwise causes a right axis deviation while rotation counter-clockwise causes a left axis deviation.

DISCUSSION

The results of the experimentally produced bundle-branch block were opposite to those obtained by Lewis in a dog, and confirmed Wilson and Barker's prediction that bundle-branch block in man would have a configuration opposite to that found in the classical interpretation.

The extrasystoles with the heart in normal position were similar to those found by Barker with the exception of Point 2 on his heart, where there was inversion in all three leads. In six of the eight cases in our series they were found to be inverted in Lead I and up in Lead III. In two cases, we obtained curves similar to those obtained by Barker, i.e., down in all three leads by stimulating Point 2.

The effect of shifting the human heart confirms Barker's prediction that what had been considered to be a right axis deviation was in reality a left axis deviation, and what was really a left was a right axis deviation. A number of factors enter into the question of shifting the heart. This problem will be taken up in more detail in a later paper.

The eight subjects chosen for study were those giving the most nearly normal electrocardiograms. In all of these cases after revival of the

heart the tracings showed either a normal or a left axis deviation (old terminology). In some of the other hearts not included in the series in which the axis deviation was to the right, resulting from abnormal position of the heart or from failure of a portion of the left ventricle to revive, we obtained evidence which indicated that the bundle-branch block may be reversed from the usual results obtained in man. The results suggest that both bundle-branch block and localization of ventricular extrasystoles cannot be localized without knowledge of the axis deviation. Further studies in this regard will be reported later.

All of the hearts in which the electrocardiogram was normal had no pericardial adhesions, and yet they gave curves similar to those obtained from a patient who did have pericarditis by Barker, Macleod and Alexander. This is evidence, we believe, that pericarditis in the hearts studied by other observers had no influence on the electrocardiogram.

Modified forms of curves of bundle-branch block occurring in experiments where the contact of the heart was through the left ventricle indicate that under experimental circumstances at least the factor of contact of the ventricle is important. Further studies in this connection will be reported later.

In some experiments before the question of position of the heart was considered, curves which resembled more closely those of the conventional interpretation were obtained. Only, however, when care was taken to see that the heart was in the normal position did we uniformly obtain the type of curves described in this paper.

SUMMARY

Eight cases of revived human heart in which a reasonably normal type of electrocardiographic curve was obtained have been studied with regard to both the localization of extrasystoles and bundle-branch block.

With the heart in normal position it is found that the extrasystoles were similar to those described by Barker, Macleod and Alexander.

The right and left bundles were cut in five instances, and the results indicate with the heart in normal position that a lesion of the right bundle is characterized by a deflection that is downward in Lead I and upward in Lead III.

When the left bundle was cut with the heart in normal position or with left axis deviation, the electrocardiographic curve was characterized by an upward deflection of the complex in Lead I and a downward deflection in Lead III.

Changes in position of the heart greatly modify the character of the curves of both extrasystoles and bundle-branch block.

Shifting of the human heart to the left in one instance gave a right axis deviation (old terminology); shifting of it to the right gave a left axis deviation. Rotation of the heart also causes variation in the electrical axis.

The authors wish to express their appreciation to the Department of Pathology, especially to Dr. Walter Siebert, and to the coroners of St. Louis and St. Louis County for their cooperation and assistance in this work.

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THE EFFECT OF POSITION OF THE HEART ON THE ELECTROCARDIOGRAM

II. Observations Upon the Electrocardiogram Obtained From a Dog's Heart Placed in the Human Pericardial Cavity*

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THE work of Oppenheimer and Pardee,[1] Farr[2] and especially Barker, Macleod and Alexander[3] indicates that there is a difference between the human electrocardiogram and the so-called classical interpretation. Cutting of the bundles in the revived human heart has definitely established the character of the electrocardiographic curves in man. Since the so-called classical interpretation of the electrocardiogram was obtained by experimental studies on the dog, an explanation of the difference of the curves from those obtained in man was thus sought.

There has been some speculation but little or no experimental work concerning the difference between the shape of the electrocardiogram of man and that of the dog taken under experimental conditions. Two main theories have been advanced. The most widely quoted one is that there is an inherent difference in the hearts themselves. It has also been suggested that there is a variation in the relationship of the heart to the surrounding structures.

Our attention was first directed to the subject while studying the electrocardiogram of dogs with experimentally produced fibrous pericarditis. In several of the animals, induced extrasystoles closely resembled those occurring in man. It was noted in the animals that the heart remained in the anterior mediastinum when the dog was on its back and the sternum was split, whereas in the usual experimental preparation with normal dogs the heart falls posteriorly.

From the work of Ackerman and Katz[4] the profound effect on the electrocardiogram of changing the position of the heart was known. We therefore decided to study the electrocardiogram of the dog's heart in its normal position. The position was determined by x-ray studies of dogs both with the chest opened and with the chest closed. It was found that the normal position of the dog's heart is in the anterior mediastinum, but when the animal is placed on its back, and the sternum split as in the usual experimental preparation, the heart falls a considerable distance in the posterior mediastinum. (Fig. 1.) It also usually rotates in a clockwise manner.

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Studies of the change in the electrocardiogram of the dog, with the heart in its normal position in the anterior mediastinum, were made by two methods. In one the entire preparation was inverted so that the heart returned to its normal position in the anterior mediastinum. In the second method the animal was placed on the animal-board on its abdomen, and the heart was approached through the posterior mediastinum. With the heart in the normal position it was found that the curves resembled more closely those obtained from the human heart. Consideration of these facts led to the investigation of the dog's heart in the human pericardial cavity.

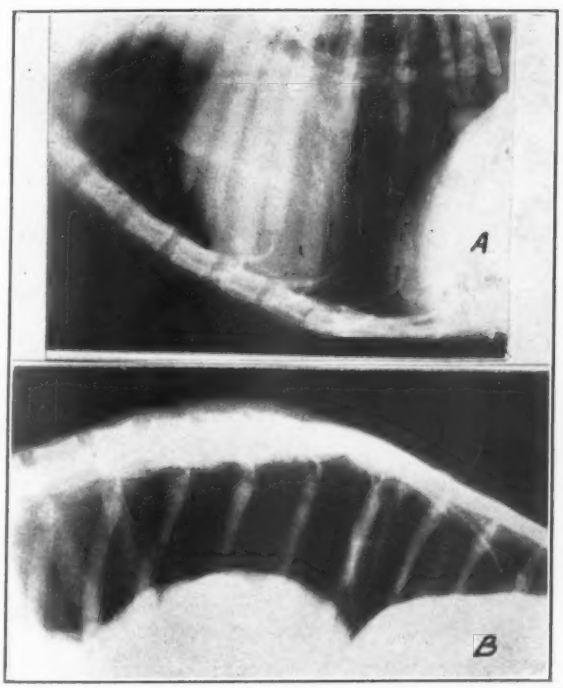

Fig. 1.—*A*, Photograph of the x-ray picture with the dog on its abdomen with the chest closed; *B*, an x-ray picture of the same animal with the chest opened and the body in the usual experimental position. Note the heart is displaced in the posterior chest in *B*.

METHOD

Human bodies were taken soon after death, and the chest was opened by a longitudinal incision which exposed the heart. Careful note was made of the position of the septum. The heart was then split along the longitudinal axis, and the anterior half was removed, leaving the posterior half in the pericardium.

A heart-lung preparation was then made by the method of Starling. It was dissected free from the body of the dog, and the dog's heart

was placed in the exact position occupied by the human heart. This necessitated certain precautions. Care was taken that the septum of the dog's heart approximated the septum of the posterior portion of the human heart. Likewise the anterior septum was placed in the

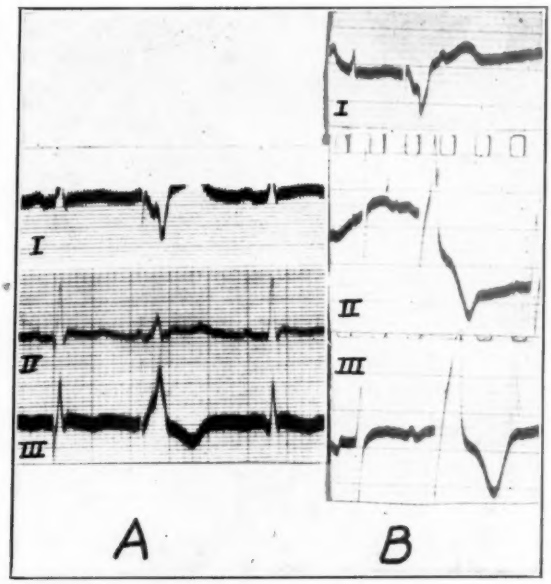

Fig. 2.—*A*, Curve obtained from the human heart; *B*, curve obtained from stimulation of Point 1 of Barker of a dog's heart placed in the human pericardial cavity.

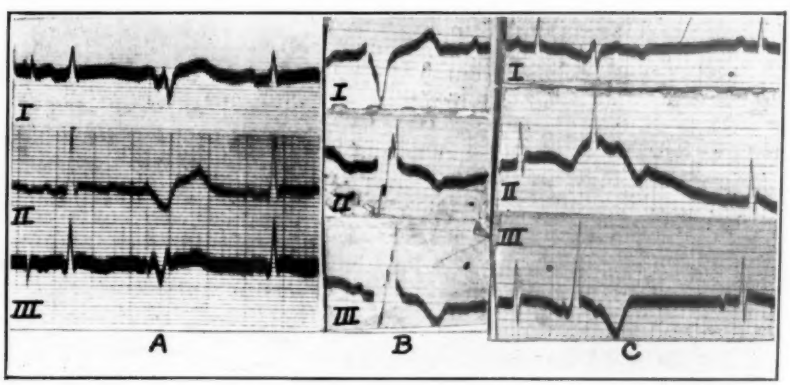

Fig. 3.—*A*, Curve obtained by Barker on stimulation of the human heart; *B*, curve obtained from a revived perfused human heart upon stimulation of the lateral wall of the left ventricle in the region of Point 2; *C*, extrasystole obtained from a dog's heart in a human pericardial cavity when Point 2 of Barker was stimulated.

exact position as that previously occupied by the anterior septum of the human heart. Care was also taken that the heart was in the same general plane in the pericardium, which occasionally necessitated removal of the sternal ends of the clavicles to permit the cannulas to

lie below them. The hearts were stimulated at the 10 points on the anterior surface designated by Barker, Macleod and Alexander,[3] and also on the posterior surfaces of the ventricles. Also the right and left bundle branches were cut. Standard leads were taken from the extremities of the cadaver.

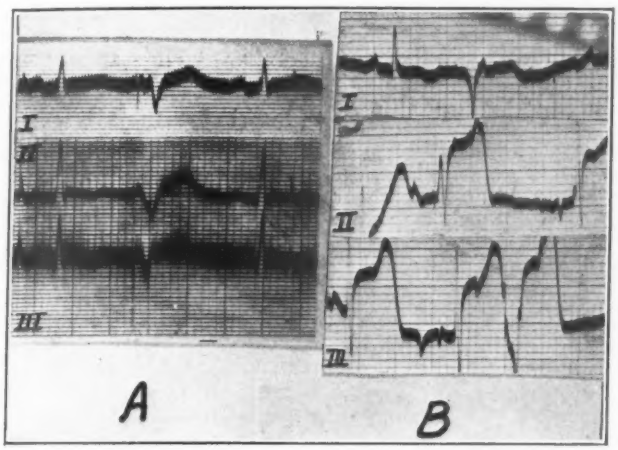

Fig. 4.—*A*, Curve obtained by Barker on stimulation of the apex of the left ventricle; *B*, curve obtained by stimulation of the apex of the left ventricle of a dog's heart in the human pericardial cavity.

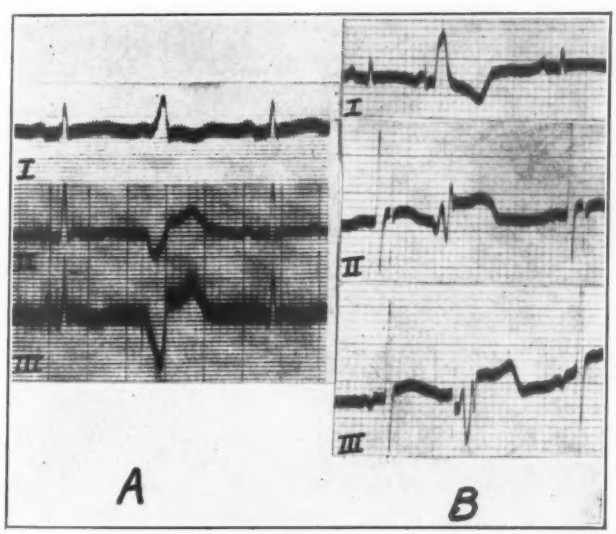

Fig. 5.—*A*, Curve obtained by Barker on stimulation of Point 4 of the right ventricle in man; *B*, curve obtained by us from a dog's heart placed in a human pericardial cavity on stimulation of the same point.

RESULTS

Stimulation of Point 1, which is located on the lateral surface of the left ventricle, gave a complex which was down in Lead I and up

in Leads II and III, similar to that obtained by Barker and by us in man.

Stimulation of Point 2 was found to be somewhat variable. Barker in his case obtained complexes which were down in all leads. We obtained a record which was inverted in Lead I and upright in Leads II and III. Since we obtained similar curves in six out of eight cases

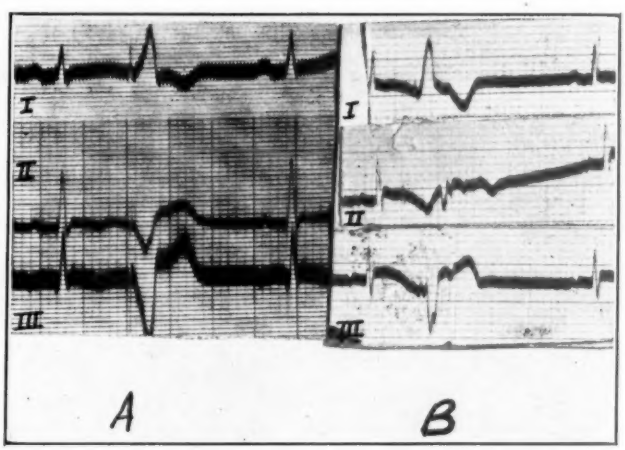

Fig. 6.—*A*, Curve obtained from the human heart; *B*, curve obtained on stimulation of Point 5 of Barker of a dog's heart placed in a human pericardial cavity.

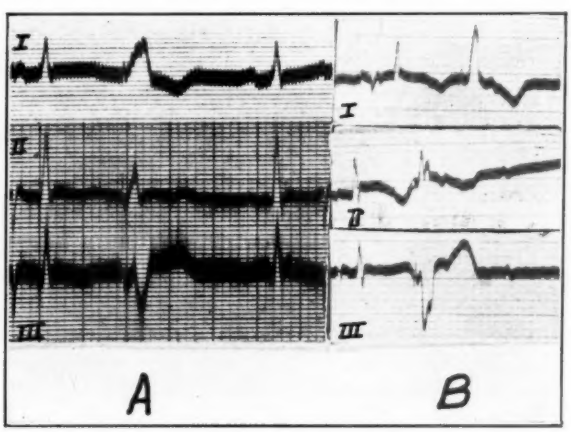

Fig. 7.—*A*, Curve obtained by Barker on stimulation of Point 7 in man; *B*, curve obtained from a dog's heart in the human pericardial cavity by stimulation of the same area.

in man, we believe that such a curve resembles more nearly the human curve which arises from the midportion of the lateral wall of the left ventricle. Extrasystoles arising from Point 3 were inverted in all leads.

Points 4, 5, and 7 on the anterior surface of the right ventricle when stimulated showed extrasystoles, whose deflection was up in Lead I

and down in Lead III. These were similar to those obtained by Barker, and also by us in the revived perfused human heart.

Extrasystoles arising from Point 9 showed a slight variation from those of the human heart in some of these experiments. In the human hearts the complex was found to be up in Leads I and II and down

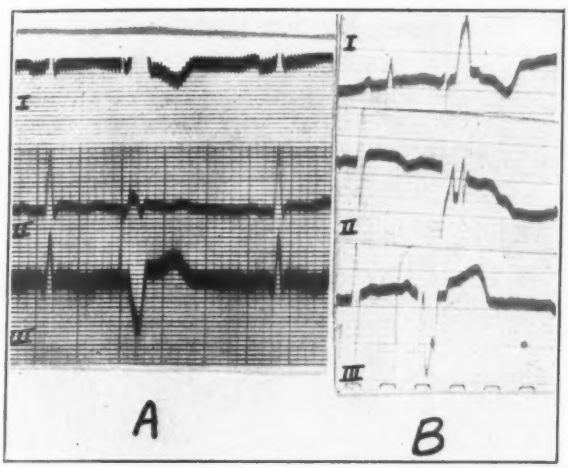

Fig. 8.—*A*, Curve obtained by Barker upon stimulation of Point 9 in the human heart; *B*, curve obtained by us on stimulation of the same area of a dog's heart within a human pericardial cavity.

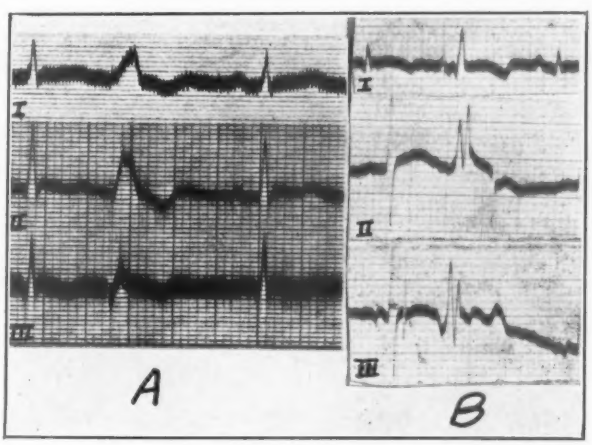

Fig. 9.—*A*, Curve obtained by stimulation of Point 10 in man; *B*, curve obtained from a dog's heart in the human pericardial cavity, by stimulation of the conus of the right ventricle.

in Lead III. In some experiments with the dog's heart in the human chest a change was found in Lead I. In this lead the R-wave was prominent, although the Q-wave was definitely down. The T-wave was deflected downward, however.

Extrasystoles arising from Point 10 which is on the conus of the right ventricle were always deflected upward in all three leads, similar to the curves obtained in the human hearts.

The dog's heart in the human chest in the position occupied by the normal human heart produced electrocardiograms when the left bundle was cut similar to those obtained previously by cutting the left bundle in two cases of the revived perfused human heart. The initial ventricular deflection was up in Leads I and II and down in Lead III.

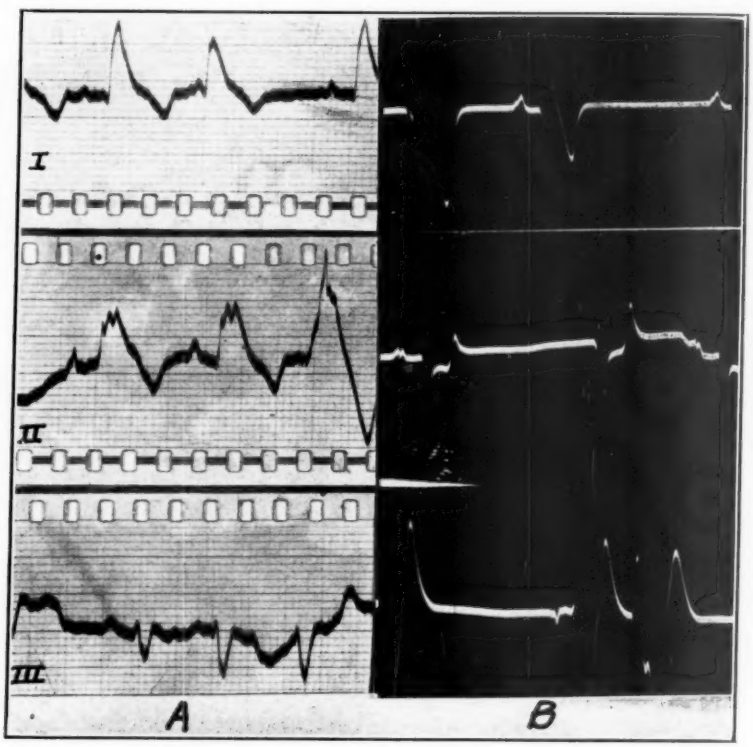

Fig. 10.—*A*, Electrocardiogram obtained after section of the left bundle branch in a dog's heart placed in a human pericardial cavity; *B*, curve obtained after section of the left bundle branch in a revived perfused human heart.

When the right bundle was cut, the initial ventricular deflections were in the same general direction as those obtained by cutting the right bundle branch in the revived perfused human heart, with the exception that in Lead II the R-wave was high, the deflections were down in Lead I and up in Leads II and III.

DISCUSSION

It is worthy of note that when the dog's heart was placed in the human pericardial cavity in such a way as to give marked right axis

deviation to the electrocardiogram, there was a complete reversal of extrasystoles from the Wilson and Barker type to those more nearly resembling the classical interpretation. The interpretation of these results will be considered in a later paper.

Minor changes from human curves occurred with the dog's heart placed in the human pericardial cavity in some experiments. These changes, we believe, are due to differences in contact of the dog's heart in the human chest, rather than to inherent differences in the hearts of the two species. This contention is supported by the fact

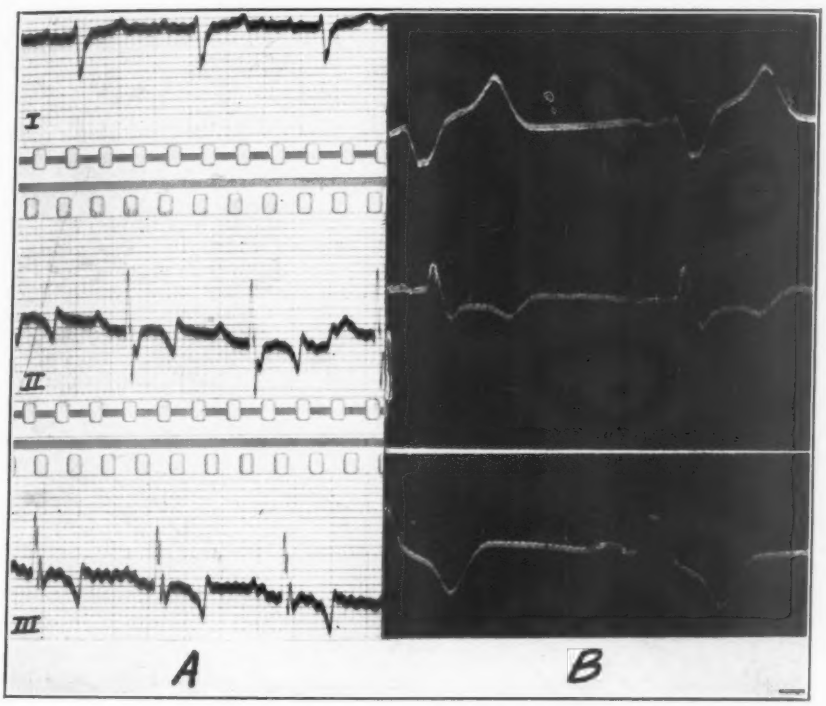

Fig. 11.—*A*, electrocardiogram obtained after section of the right bundle branch of a dog's heart placed within a human pericardial cavity; *B*, electrocardiogram of a revived human heart after section of the right bundle branch.

that when changes in the character of extrasystoles or bundle-branch block occurred, there was usually some variation in the electrical axis.

The conclusion drawn from these experiments is that the chief difference between the electrocardiogram of the dog under experimental conditions and of man is due to the position of the dog's heart in the chest. In the dog the thorax has a relatively deep anteroposterior diameter, which, when the animal is on its back in the usual experimental preparation, permits the heart to be displaced from its natural position when the chest is opened. In man the chest is narrow and the heart does not shift. Consequently in the usual experimental position

in the dog, one may obtain an electrocardiogram which is atypical. There is no indication that this is due to intrinsic differences between the dog's heart and that of man.

SUMMARY

Since the human heart in normal position gives curves dissimilar to those found in the dog under experimental conditions, and since there is a marked difference in the shape of the chests in the two species, the beating dog's heart was placed within the human pericardial cavity, and the electrocardiograms were compared.

It was found that under such circumstances the dog's heart yielded curves which were similar to those obtained with the revived beating human heart.

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THE EFFECT OF POSITION OF THE HEART ON THE ELECTROCARDIOGRAM

III. Observations Upon the Electrocardiogram in the Monkey*

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THE difference between the electrocardiographic curves obtained in the dog under experimental conditions and those in man have been pointed out by a number of observers.[1, 2] The similarity of the electrocardiographic curves obtained from a dog's beating heart placed within the human pericardial cavity in a normal position makes it appear that the chief difference between the electrocardiogram of man and that of the dog under experimental circumstances is due to difference in the relationship of the heart to the chest, rather than to a difference in the heart. It has been pointed out that the chest of the dog has a relatively wide anteroposterior diameter and when the chest is opened with the animal on its back there is considerable displacement and rotation of the heart. This cannot occur in man with a normal chest.

It was therefore considered important to choose an animal the shape of whose chest resembled more closely that of man, and whose heart like that of man was not displaced when the chest was opened. It was found that the chest of the monkey, although not identical to that of man, resembled more closely the human thorax than did that of the dog. The monkey was, therefore, used for study.

So far as we have been able to determine, the electrocardiogram has been recorded in only two monkeys. Wilson and Herrmann[3] studied bundle-branch block in a single monkey of the genus Cercopithaeus, and found concordant curves when the right bundle was cut. Lewis[4] studied a Rhesus monkey with experimentally produced right bundle-branch block. He obtained a discordant curve when the right bundle was cut. The character of the curve was up in Lead I and down in Lead III. Lewis was unable to explain this curve and suggested that further observations be made.

Nine monkeys were studied, eight of which were of the genus Rhesus, and one Cebus. Each animal was anesthetized, a tracheal cannula inserted, and artificial respiration begun. The chest was opened by splitting the sternum, and the pericardium was opened by a longitudinal incision. Electrocardiographic tracings were taken with the regular leads.

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Ventricular extrasystoles were produced by stimulating the twelve points of Barker and the sides of the septum by applying the electrode directly to it. In one of the experiments we were able to cut the left bundle and in two, the right bundle.

The effect of rotation of the heart in several planes was also studied; that is, displacement to the right, to the left, and rotation of the heart clockwise and counter-clockwise. The degree of displacement and rotation was roughly determined by means of a semicircular disc nine inches in diameter on which were marked the degrees of displacement from the midline of the body.

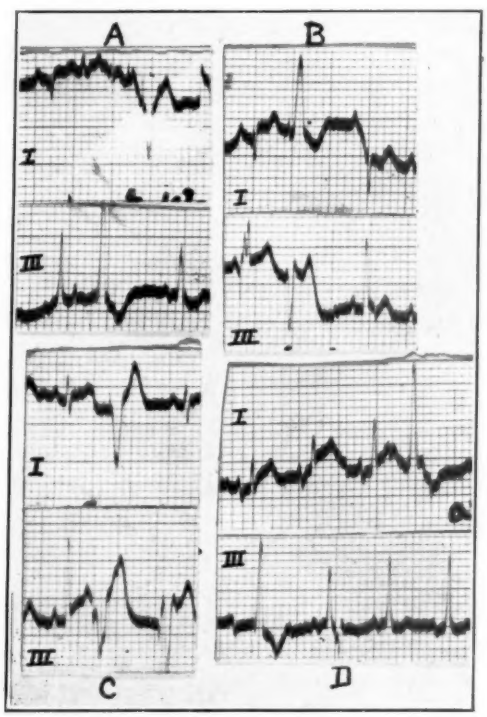

Fig. 1.—*A* and *B*, discordant curves obtained by stimulation of the ventricle of the monkey heart. *A*, was obtained from the left ventricle; *B*, from the right. *C* and *D* represent concordant curves obtained by stimulation of the apex and conus, Leads I and III only.

RESULTS

When the chest of the monkey was opened, with the animal on its back, it was noted that the heart, like that of man, did not fall into the posterior mediastinum as it does in the dog. It was also found more difficult to displace the heart from its normal position than in the case of the dog. With the heart in its normal position four general types of extrasystoles were obtained, which were similar in most instances to those found in man.

Concordant extrasystoles were obtained by stimulating the apex of the left ventricle in the region of Point 3 of Barker. The curve was found to be inverted in all leads, but was lowest in Lead III. Occasionally, Point 2 gave concordant curves (Fig. 1).

Concordant curves were obtained by stimulating the conus of the right ventricle, and were obtained also from a proportionately larger area of heart than that in man. It embraced Points 7, 9, and 10 of

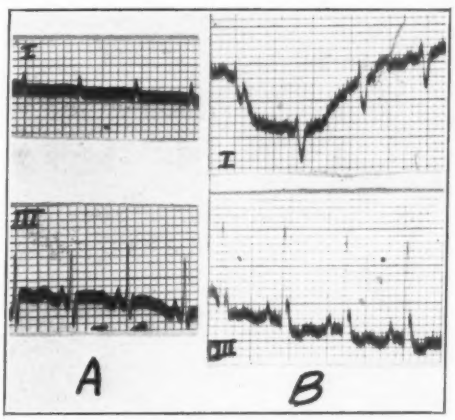

Fig. 2.—*A*, The normal curve, Leads I and III; *B*, the electrocardiogram obtained after section of the right bundle branch in the heart of a monkey.

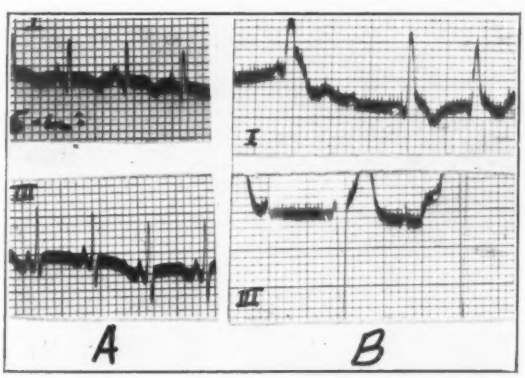

Fig. 3.—*A*, The normal electrocardiogram of a monkey with thorax open, Leads I and III; *B*, the curve after section of the left bundle branch.

Barker. The curves were up in all leads, usually highest in Lead III (Fig. 1 *D*).

Discordant curves were obtained by stimulating the lateral wall, the anterior surface close to the septum, the posterior surface, and inside of the left ventricle. In two instances, the curve resulting from the stimulation of Point 2 of Barker on the left ventricle was inverted in Lead III instead of being upright. The extrasystoles arising from

TABLE I*

MONKEY	POSITION OF HEART	CHARACTER OF COMPLEX											
		LEAD I				LEAD II				LEAD III			
		QRS		T		QRS		T		QRS		T	
1	Normal	up	4	up	1	up	3	up	1	up	3	up	1
	67-Left	down	8	up	3	up	6	isoelectric		up	12	down	4
	45-Right	up	15	down	5	up	8	down	3	up	3	up	2
	Counter-clockwise	up	5	down	2	up	4	up	1	down	8½	up	2
	Clockwise	down	8	up	1	down	7	up	3	down	7	up	3
	Apex-up	up	7	down	2	up	5	down	5	up	5	down	3
2	Normal	up	3	up	1	up	2	up	½	down	3	up	½
	45-Left	down	4	up	2	down	4	up	1	∫up	4	∫up	1
										⌋down	6	⌋down	1
	65-Right	up	6	up	½	down	4	isoelectric		down	4	up	1
	Clockwise	up	1	up	½	down	9	up	3	down	10	up	3
	Counter-clockwise	up	3	up	1	down	8	up	2	down	10	up	2
3	Normal	up	1	isoelectric		down	2	up	1	down	3	isoelectric	
	65-Right	up	3	isoelectric		up	12	up	1	up	13	down	1
	65-Left	down	5	down	1	up	4	down	1	up	9	isoelectric	
	Rotated counter-clockwise	isoelectric		isoelectric						up	2	isoelectric	
	Clockwise	down	4	up	½	∫up	1	isoelectric		up	2	down	½
						⌋down	1						
	Rotated clockwise	up	1	isoelectric						down	2	isoelectric	
4	Normal	up	1	down	1	up	3	–		up	4	–	
5	Normal	up	2	isoelectric		∫R-up	2	up	½	down	3	up	1
						⌋S-down	2						
	45-Left	down	2	up	1	up	4	isoelectric		up	6	isoelectric	
	67-Right	up	7	down	1	up	10	down	½	up	4	isoelectric	
	Clockwise	down	3	up	½	down	4	up	1	∫R-up	1	isoelectric	
										⌋S-down	1		
	Counter-clockwise	up	2	isoelectric		up	3	up	1	up	2	up	1
	Apex-up	isoelectric		isoelectric		up	4	up	½	up	4	up	½
	Apex-down	down	½	isoelectric		down	4	down	4	down	5	down	1
6	Normal	up	5½	up	1	down	7½	up	1	down	10	up	1
	67-Left	down	4	up	2	down	5	isoelectric		down	6	up	1
	45-Right	up	1	isoelectric		up	6	up	½	up	7	up	1
	Counter-clockwise	up	4	isoelectric		down	5	up	3	down	6	up	3
	Clockwise	up	1	up	½	down	8	up	2	down	9	up	2
	Apex-up	up	2	isoelectric		down	2	up	1	down	5	up	1
	Apex-down	up	4	down	½	down	11	up	3	down	9	up	4
7	Normal	up	2	up	1	up	2	up	1½	down	5	up	3
	45-Left	up	1	up	2	up	4	up	2	up	4	isoelectric	
	50-Right	up	6	down	1	up	5	down	1	up	4	up	2
	Clockwise	up	½	up	¼	isoelectric		isoelectric		down	6	up	4
	Counter-clockwise	up	2	up	½	isoelectric		isoelectric		down	4	up	1
	Apex-up	isoelectric		isoelectric		up	½	up	1	up	6	up	1
	Apex-down	up	2½	up	½					down	7	up	6

TABLE I—CONT'D*

MONKEY	POSITION OF HEART	CHARACTER OF COMPLEX											
		LEAD I				LEAD II				LEAD III			
		QRS		T		QRS		T		QRS		T	
8	Normal	up	2	isoelectric		up	6	up	1	up	8	down	3
	67-Left	up	1½	up	1	up	4	up	1	up	4	up	1
	67-Right	up	3	down	1	up	10	down	1	up	13	up	1
	Apex-up	up	3	down	1	up	4	isoelectric		up	4	down	4
	Apex-down	up	3	up	1	R-up 3 S-down 3		up	1	R-up 3 S-down 6		up	2
	Clockwise	down	3	isoelectric		up	5	up	3	up	13	up	2
	Counter-clockwise	up	2	isoelectric		down	7	up	2	down	9	up	2
9	Normal	up	2	up	1	up	4	up	3	up	6	up	3
	67-Left	down	5	up	2	up	6	down	2	up	11	down	3
	67-Right	up	4	down	1	up	4	up	1	up	4	up	2
	Apex-up	down	2	down	1	up	2	up	½	up	4	up	3
	Base rt. apex normal	up	2	up	1					up	3	up	4
	Clockwise	down	1½	up	½	R-up 4 S-down 3		up	2	R-up 7 S-down 4		up	3
	Counter-clockwise	up	½	down	½	down	1	up	½	down	1	up	1

*The table consists of the results obtained by displacing the apex of the monkey heart and measuring the electrocardiogram above or below the isoelectric level in millimeters. The apex of the heart was displaced to the left and to the right. The heart was rotated clockwise and counter-clockwise. The apex was then raised so that only the base of the heart was in contact with the chest and then the apex was depressed against the spine.

the left ventricle were down in Lead I and up in Lead III with the heart in normal position (Fig. 1 *A*).

Discordant curves were also obtained by stimulating the right ventricle. They embraced the remainder of the right ventricle represented by Points 4, 5, 6, and 8 of Barker, and corresponding points posteriorly. The character was always up in Lead I and down in Lead III. Stimulation of the septum of the right ventricle gave similar curves (Fig. 1 *B*).

Bundle-Branch Block.—Cutting of the right bundle in the monkey did not substantiate the findings of Lewis. Discordant curves were obtained, which were down in Lead I and up in Lead III. Cutting of the left bundle in one instance produced a curve that was up in Lead I and down in Lead III.

The effect of rotation of the heart in these animals was studied both from the standpoint of axis deviation and from the effect on position of extrasystoles and may be seen in Table I.

Displacement of the heart to the right tends to cause the initial ventricular deflections to be low in Lead I, and more upright in Lead III. Rotation of the heart in a clockwise manner tends to cause a right axis deviation, and rotation counter-clockwise causes a left axis deviation. It is also of interest to note that lowering of an inversion

of the T-wave in Lead I with an elevation of the T-wave in Lead III was frequently seen with left axis deviation produced by counter-clockwise rotation.

DISCUSSION

In all the experiments, results from stimulation of the outer surface of the ventricles produced extrasystoles similar to those obtained in man. An exception to this is that the area, particularly at the base of the right ventricle from which concordant curves are obtained, is increased compared to man. Stimulation of the septum of the ventricle of the monkey in two instances produced extrasystoles similar to those obtained on the outer surface of the heart.

The relative increase in size of the area from which concordant extrasystoles were obtained in the monkey, as compared to that of the dog and the man, indicates that the spread of the impulse from within outward is over a greater area. With such results one would be led to believe that some difference may exist in the relationship of the base of the heart to the right bundle when compared to that of man.

The observation made in two animals, in which the inside of the ventricles was stimulated, indicates that extrasystoles on the inside and outside of the heart are similar, depending upon the location with relation to the electrical axis.

The results obtained from rotation of the heart are instructive, and suggest that rotation of the heart may be an important factor in explaining axis deviation. Experimentally, counter-clockwise rotation or displacement of the heart to the right causes left axis deviation on the electrocardiogram. Clockwise rotation of the heart or displacement of the heart to the left causes a tendency to right axis deviation. The explanation of the axis deviation must be due to changes in relationship of the septum of the heart to the body of the animal. In view of the increase in size of the muscle mass of the left ventricle in hypertrophy, these findings suggest that the cause of axis deviation may be due to displacement of the septum to the opposite side. Thus, in left ventricular hypertrophy, the septum would be displaced to the right, while in right ventricular hypertrophy the septum would be displaced to the left.

Furthermore, the changes in the human electrocardiogram that have been described by Luten and Grove[3] in man have thus been produced experimentally in the monkey. These authors suggested that the electrocardiogram in which the QRS complexes were up in Lead I, and down in Lead III, with inverted T-wave in Lead I, and upright T-wave in Lead III, was due to vascular changes in the heart which led to changes in conduction. Our experiments, on the other hand, indicate

that the changes may be due to a change in the position of the heart in which the organ is rotated counter-clockwise, and the septum is shifted to the right.

These findings substantiate our previous work showing that an animal, with a relatively narrow anteroposterior diameter of the chest in which the heart position is not displaced with rotation when the chest is opened, gives an electrocardiogram similar in most respects to that of man.

SUMMARY

1. Observations were made upon nine monkeys, with chest of similar contour to that of man. Electrocardiograms of bundle-branch block and extrasystoles resembled those obtained from man.

2. Change of position of the heart was also studied in the monkey, and it was found that rotation of the heart clockwise produced right axis deviation (old terminology), while rotation counter-clockwise produced left axis deviation. Displacement of the heart to the left caused right axis deviation; displacement to the right caused left axis deviation.

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THE COURSE OF RHEUMATIC HEART DISEASE IN ADULTS*†‡

III. The Influence of Auricular Fibrillation on the Course of Rheumatic Heart Disease

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THE usual method of treating statistically data on auricular fibrillation is to take as a base records of an unselected group of patients, all of whom present auricular fibrillation, in order to arrive at conclusions concerning the incidence, prognosis, and other phenomena pertaining to this irregularity. The data are usually classified as to etiology, valvular lesions, age at first observation and sex.[1-10] Although a great deal of valuable information has been contributed by this method of study, the exact meaning of auricular fibrillation in the course of any one of the heart diseases cannot be known until it (auricular fibrillation) is studied as an incident in the course of that etiological class. This it is proposed to do now in the case of rheumatic heart disease.

The basic data in this analysis are the same as those used in two previous papers on the course of rheumatic heart disease.[11, 12] The sources are the records of patients followed in the ten-year period 1921-1931 in the adult cardiac clinic at Bellevue Hospital, in the wards of the Third Medical Division of Bellevue Hospital and in private practices.§ It has been possible to compare the course of this form of heart disease in the presence both of auricular fibrillation and of sinus rhythm. The histories of patients who did not develop the irregularity at any time form a group for comparison.

INCIDENCE

Of the 1,633 cases of rheumatic heart disease reviewed, 445 patients (27.3 per cent) developed auricular fibrillation, but of the 644 patients who died, 276 (42.8 per cent) were known to have done so. The latter

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‡This research was made possible through a grant from the Metropolitan Life Insurance Company. The Heart Committee acknowledges gratefully this cooperation.

§The practices of Dr. John Wyckoff and of Dr. Arthur C. DeGraff have been utilized for this purpose. We are indebted to Dr. Wyckoff for the use of many records and for his supervision of our analyses in many cases.

number probably represents the true incidence, since the whole course is known in these cases. It is on the records of the 644 deceased patients that this study is based.

The type of valvular lesion seems to have some effect on the incidence of auricular fibrillation. In agreement with other observers,[6, 13] the highest incidence was found among patients with mitral stenosis (50.5 per cent). When mitral stenosis was accompanied by aortic valvular lesions, the incidence was lower (27.5 per cent) but not so low as that found by Lewis.[13] He states that whether aortic insufficiency appears alone or in combination with mitral stenosis, the incidence of auricular fibrillation is low—less than one case in fifty. The difference in inference can be explained only in part. The entire history of our patients is known. Lewis' were not; he studied the records of his clinic during an arbitrarily limited period and may have included patients who developed auricular fibrillation later.

In the case of the rarer valvular lesions the groups were too small to warrant judgments based on statistical analyses, although the data presented by them may indicate trends. When mitral insufficiency appeared alone, auricular fibrillation was less frequent than in the presence of various combined lesions (16.6 per cent against 41.5 per cent). Though the group of cases of aortic valvular disease, uncomplicated by other valvular lesions, numbers only eight, the fact that one-half developed auricular fibrillation is significant in view of Lewis' statement as to its rarity.

Sex Incidence.—The importance of considering the relationship of auricular fibrillation to a particular etiological type of heart disease is brought out clearly when the sex incidence is examined. When they studied a total group of cases of auricular fibrillation, Stroud, La Place and Reisinger[7] found a preponderance of 30 per cent in favor of males, while Cookson[1] reported a ratio of 2 to 1 in favor of females. In neither instance was it studied in its relation to the kind of heart disease, nor was there available for comparison a group of patients with sinus rhythm. When the proportion of males to females afflicted with rheumatic heart disease who developed auricular fibrillation is compared, no great difference is found. Among males 41 per cent, among females 45.7 per cent developed auricular fibrillation. When mitral disease was present without aortic involvement, the incidence was slightly higher in males (51.5 per cent against 48 per cent). When aortic disease was present with or without mitral involvement, the incidence was slightly higher among females (36.8 per cent against 24.8 per cent).

AGE

Age at Onset.—Patients can often name the exact date, and frequently the hour, when auricular fibrillation began. In almost three-

fourths of the patients this arrhythmia was already present when they came under observation (Fig. 1). Careful questioning made it appear unlikely that the condition had existed for any length of time. Campbell[9] has called attention to the fact that the onset of the irregular ventricular rhythm of auricular fibrillation enters into the patient's con-

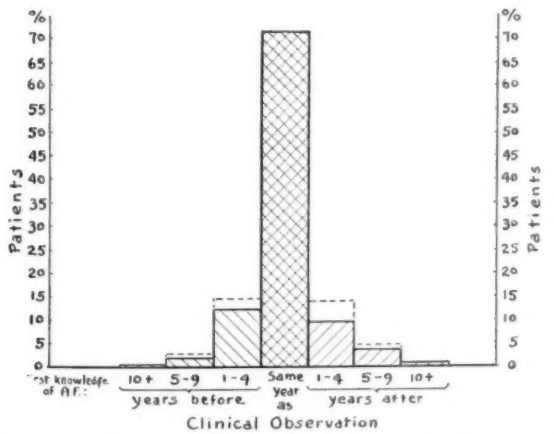

Fig. 1.—Interval between first knowledge of auricular fibrillation and clinical observation of patients.

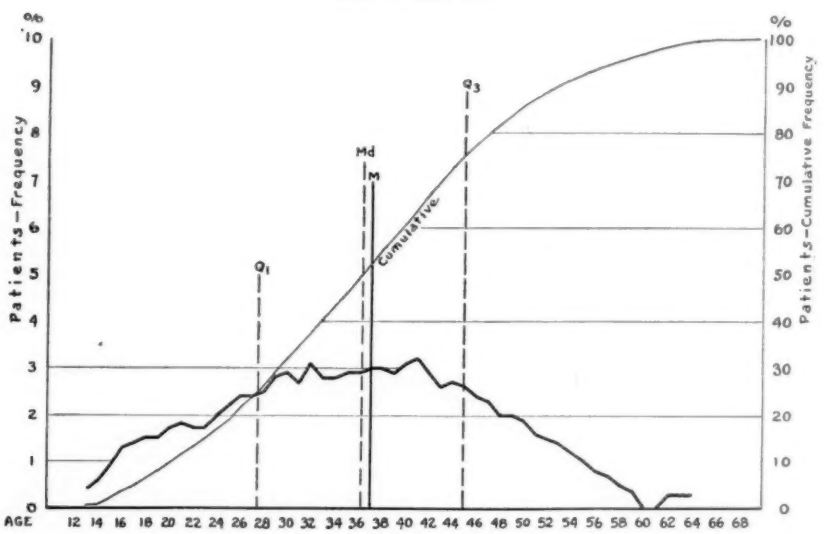

Fig. 2.—Age at first knowledge of auricular fibrillation.

sciousness to such a degree that he usually seeks immediate medical attention. With this judgment we agree. The date assigned for the onset of auricular fibrillation is in all probability, therefore, very close to the actual one. The arrhythmia was known to be present for a year or more before examination in 14 per cent, and developed under observation after a year or more in 13.5 per cent. Auricular fibrillation

existed in a small group (14 cases) in the paroxysmal form. No attempt was made to separate the paroxysmal from the persistent form, since many patients eventually developed the continuous form, and all suffered from organic heart disease. The diagnosis was in each case confirmed by an electrocardiogram.

The median age at which the patients first developed auricular fibrillation was 36 years, the mean age 37, and the interquartile range between 27 and 45 years (Fig. 2). The arrhythmia was most commonly observed in the fourth decade (30.4 per cent) and especially the second half (15.9 per cent). A comparison of this curve with those describing the general progress of rheumatic heart disease[11] suggests at once that auricular fibrillation occurs late in its course.

Age at Death.—The age at death was, on the average, higher when auricular fibrillation existed than when the sinus rhythm was present

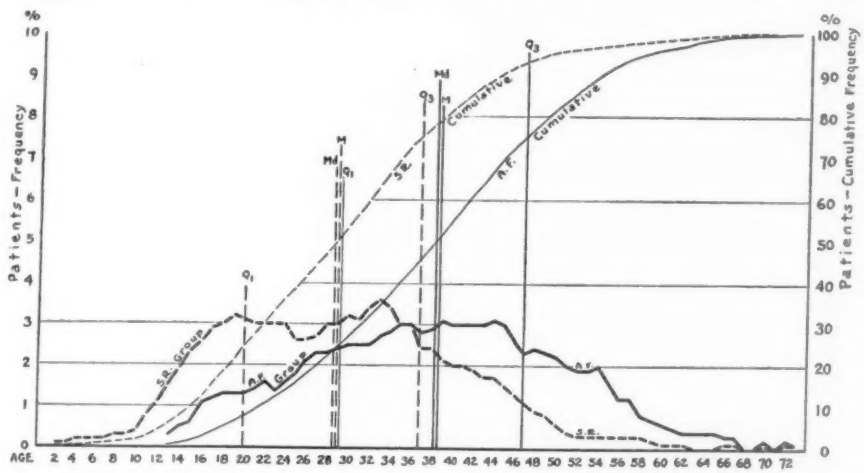

Fig. 3.—Age at death in auricular fibrillation and sinus rhythm groups.

throughout life (a mean of 38 years against 29 years, Fig. 3). The mode fell much earlier in the latter and suggests, again, that auricular fibrillation occurs among patients who enjoy a relatively longer life span.

OTHER RELATIONSHIPS

Relation to Initial Rheumatic Infection.—The age at initial infection does not predispose to the onset of a particular cardiac rhythm. It was about the same when the sinus rhythm persisted as when auricular fibrillation developed before death (Fig. 4). Patients who were infected early fell subject to auricular fibrillation as often as those infected later in life except when the initial infection occurred after thirty; the incidence then was slightly higher. Of patients infected before age ten, 39.4 per cent; between 10 and 14 years, 35.6 per cent;

between 15 and 19 years, 44.6 per cent; between 20 and 29 years, 41.4 per cent; and of those infected at 30 years or later, 48.4 per cent developed auricular fibrillation.

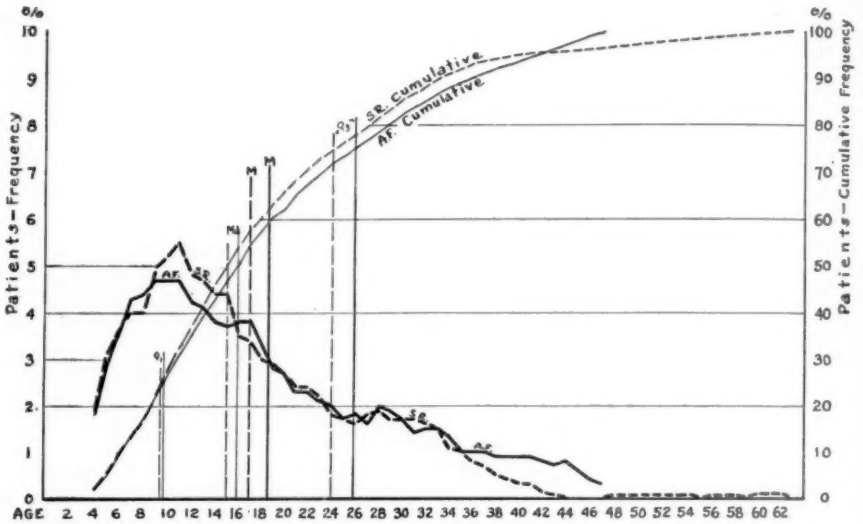

Fig. 4.—Age at initial infection in auricular fibrillation and sinus rhythm groups.

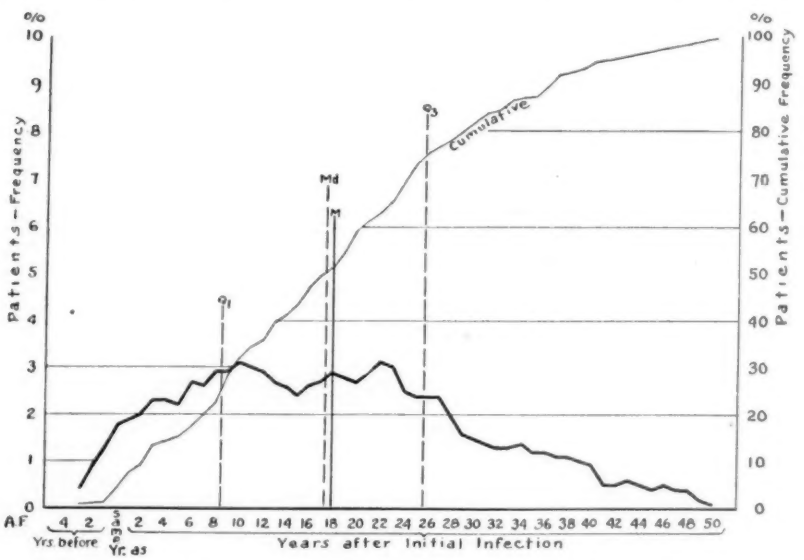

Fig. 5.—Interval between initial infection and onset of auricular fibrillation.

In view of the fact that the mean duration of life after the onset of infection in rheumatic heart disease is 15 years, three-fourths being dead within 22 years,[11] the further fact is striking that patients who develop auricular fibrillation do not do so until after a mean duration

of 18 years (Fig. 5). The arrhythmia is, in short, a late manifestation in rheumatic heart disease. The duration of the disease and not the age at initial infection is the chief factor in its development.

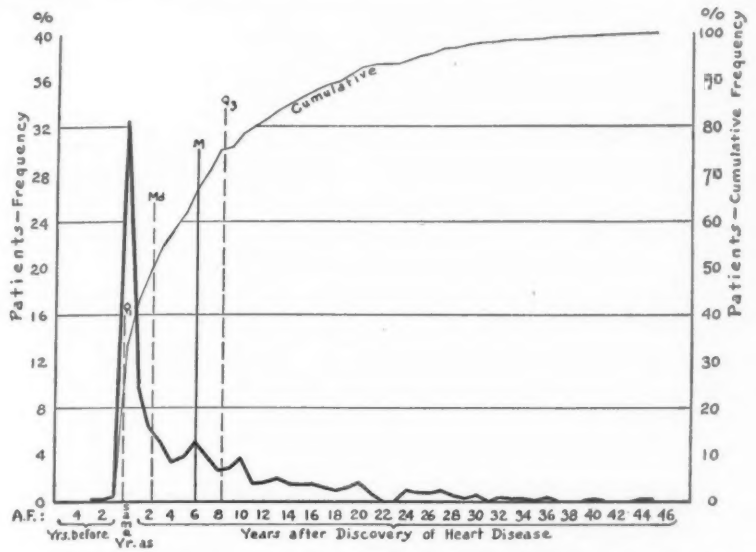

Fig. 6.—First knowledge of auricular fibrillation and discovery of heart disease.

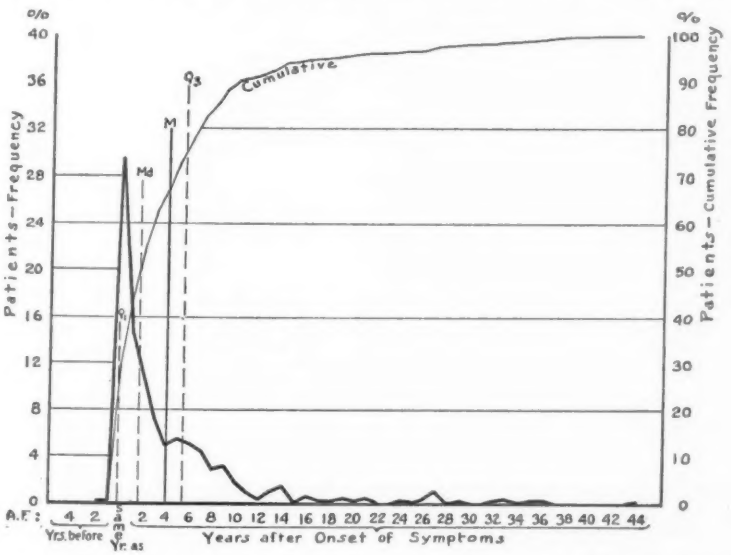

Fig. 7.—Onset of symptoms and first knowledge of auricular fibrillation.

Relation to Discovery of Heart Disease.—In rheumatic heart disease the cardiac reserve is frequently so good that for several years patients present few or no symptoms.[11] The onset of auricular fibrillation causes symptoms, however, which prompt them to seek medical advice. It is

not surprising, therefore, that the diagnosis of organic heart disease was made in the same year in which auricular fibrillation was first known to be present in nearly one-third (32.5 per cent, Fig. 6). In a few instances (0.8 per cent) it was evident that the irregularity existed before awareness of the presence of organic heart disease. On the other hand, in 25 per cent heart disease had been diagnosticated 9 or more years before the arrhythmia was noticed.

Relation to Symptoms of Cardiac Insufficiency.—Auricular fibrillation supervened, on the average, four years after symptoms of heart disease first appeared (Fig. 7), and in 25 per cent after six or more years. In 126 (29.3 per cent) both occurred in the same year.

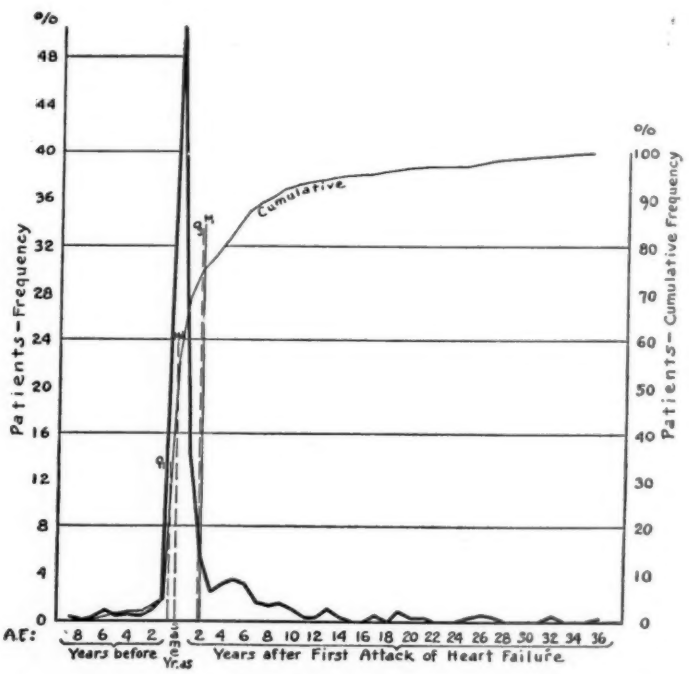

Fig. 8.—First attack of heart failure and onset of auricular fibrillation.

Relation to Congestive Heart Failure.—So far as could be learned, congestive heart failure did not occur in 17 per cent of the patients. The remainder suffered at least one attack. The mean interval between the first attack and the onset of auricular fibrillation was 2 years (Fig. 8). Both were experienced in over half the cases in the same year (51.4 per cent). This is significant in that it helps to confirm the impression that the rapid irregular ventricular rate is itself a contributing factor to the occurrence of congestive heart failure.

Duration of Life After Onset.—It is the general impression that the duration of life after the onset of auricular fibrillation is often

long.[10, 14] The time is variously estimated, but the facts here presented are at variance with this belief. Stroud, La Place and Reisinger[7] found it to be as brief as 2½ to 3 years. In our experience the mean duration was only 2 years; in many cases death took place within a year of the time that this arrhythmia began (34.3 per cent, Fig. 9). Seventy-five per cent died before the third year thereafter. Rarely, in three instances only, did patients live for 10, 11 and 12 years. For the most part, then, auricular fibrillation appears to be a terminal condition. It may be said that the chances of surviving the year in which the irregularity is first noted are fair, 2 to 1; but the chances of surviving three years are only 1 to 4, and five years about 1 to 9. It is evident both from these data and from those of Stroud, La Place and Reisinger[7]

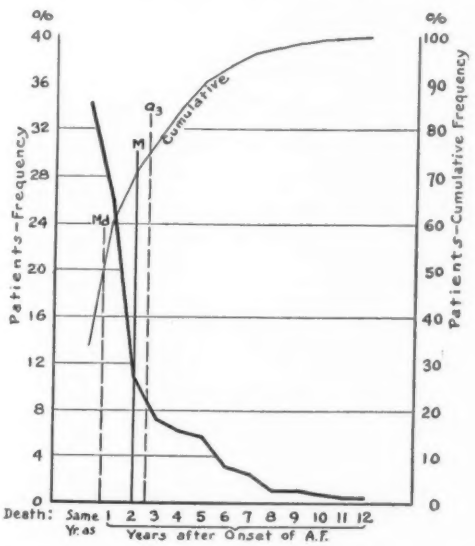

Fig. 9.—Duration of life after onset of auricular fibrillation.

that optimism as to length of life after the onset of auricular fibrillation is unwarranted statistically and that the uncontrolled observations of a few patients reported in the past have given an entirely erroneous impression as to its prognostic seriousness.

Relation of Its Incidence to Duration of Disease.—As has been pointed out, inquiry into the rôle played by auricular fibrillation in the course of rheumatic heart disease suggests strongly that the arrhythmia is more liable to occur when the disease is of relatively long standing. Support for this belief is found in the greater incidence of the irregularity in a group in which the disease has been studied to the end of its course; that is to say, in patients who have died, than in a group still living; in the fact that its onset is most frequent in the fourth decade of life; in that the age at death is, on the whole, much higher among

patients who have developed auricular fibrillation, and in the short duration of life after its onset. When its incidence in disease of short duration is directly compared with that in disease of longer duration, further evidence is forthcoming. In disease of less than ten years' duration, for instance, auricular fibrillation occurred in 27.5 per cent; when the disease lasted from 20 to 29 years, it occurred in 50 per cent; from 30 to 39 years, in 65.6 per cent; and 40 years or more, in 88.3 per cent. Its late occurrence may account for the fact that it is seen so rarely in children.[1, 6, 8]

The mean duration of life was 13 years in the group that did not, and 19 years in the group that did, develop the arrhythmia. The difference between the medians and the quartiles suggests the same in-

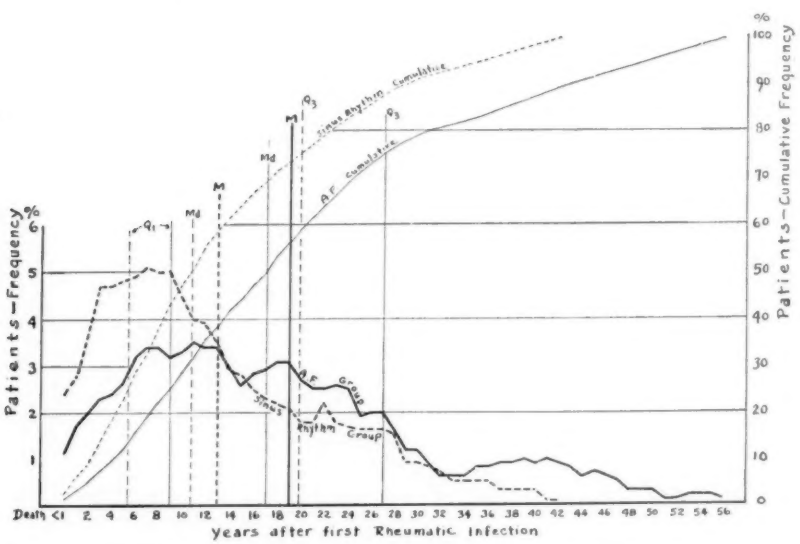

Fig. 10.—Duration of disease in auricular fibrillation and sinus rhythm groups.

ference (Fig. 10), namely, that those who live longest develop auricular fibrillation. Their longer life does not mean, of course, that patients who develop auricular fibrillation have a better prognosis, for it has already been pointed out that the arrhythmia is a late manifestation. It merely emphasizes the fact that the longer rheumatic heart disease lasts, the more likely is the patient to develop auricular fibrillation before he dies.

Influence of Rhythm on the Relation of Age at Initial Infection to Duration of Life.—The age at which rheumatic infection begins seems to be important so far as the duration of life is concerned.[11] After *four* years of illness, if infection began in the third decade, deaths are four times as frequent as if it began in the first decade, when the sinus rhythm persists; the same mortality ratio obtains in auricular fibrilla-

tion. After *fourteen* years of illness a similar mortality situation exists, except that the ratio in the older age groups is now only twice that in the younger, both when the sinus rhythm persists and when auricular fibrillation develops (Fig. 11). Obviously, as concerns life expectancy it is not the rhythm of the heartbeat that counts, for normal and auricular rhythms maintain the same relation to expectancy. The facts which are emphasized in this arrangement of curves must not be confused with the influence which the duration of the disease exerts on the occurrence of auricular fibrillation. The facts concerning this relation have already been described.

Age at Onset of Auricular Fibrillation Related to Subsequent Length of Life.—It has been stated that if auricular fibrillation appears before age 20, the duration of life after the onset is on the average less than one year.[1, 7] The data here submitted confirm these observations. When it supervened after age 20, the mean life expectancy was about 2 years (Fig. 12).* Two years are even less than the experience reported by

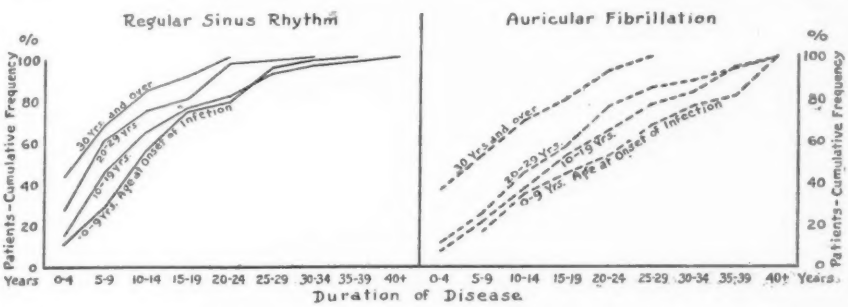

Fig. 11.—Duration of disease related to age at initial infection in fibrillation and sinus rhythm groups.

Cookson[1] and slightly less than that reported by Stroud, La Place and Reisinger,[7] in whose cases the onset is given as between ages 20 and 40. The same duration of life prevailed when the onset was after age 40, although the small group of seven patients studied by Stroud, La Place and Reisinger[7] yielded a different result. It is difficult to compare our data with theirs because they divided their cases into those in which the initial infection occurred before and after age 20. A detailed analysis is given only before age 20. Calculation shows that after age 20 the average duration was 2½ to 3 years. In the main, therefore, their results coincide with ours.

CAUSE OF DEATH

In general, whether patients with rheumatic heart disease developed auricular fibrillation or did not, they died of similar causes. In each

*Because of the small size of our sample and because of a possible unintentional bias in the sample, it did not seem expedient to calculate the probable errors of the various means referred to.

group, about 45 per cent died of congestive heart failure; in about 25 per cent more, death was described as "cardiac," although a more specific cause was not given (Fig. 13).

Bacterial endocarditis caused death among patients with auricular fibrillation in only three instances, among others in 6 per cent. Similar

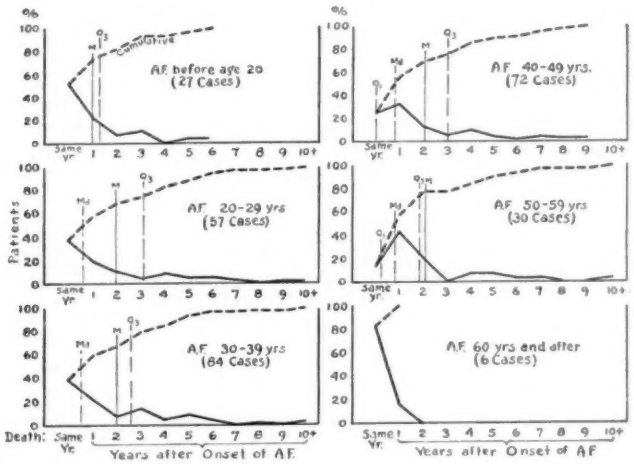

Fig. 12.—Duration of life after onset related to age at onset of auricular fibrillation.

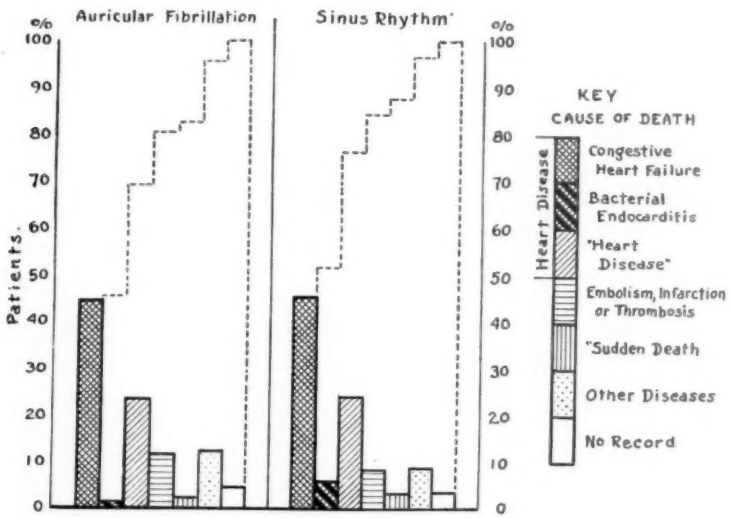

Fig. 13.—Cause of death.

observations have been recorded.[15, 16, 17] It is possible that the infrequent association of bacterial endocarditis with auricular fibrillation may be explained by the evidence already presented, that the arrhythmia is usually a late manifestation in long standing cases. As was pointed out,[11] the average duration of the disease was only nine years

among patients who developed bacterial endocarditis. It appears, then, that patients who died of subacute bacterial endocarditis have not had rheumatic heart disease long enough to develop auricular fibrillation; hence, the rare coexistence of the two conditions.

Embolism, infarction or thrombosis caused death slightly more often among patients with auricular fibrillation (11.5 per cent), however, than among others (8.4 per cent), contrary to Cookson's[1] observations.

This study suggests, then, that in both groups 70 per cent to 75 per cent of patients die a cardiac death. Other diseases, not related to the circulatory system, caused death in 12.3 per cent of patients with auricular fibrillation and in 8.7 per cent of those in the sinus rhythm group. The additional load on the circulatory system due to auricular fibrillation may, perhaps, account for the difference.

SUMMARY AND CONCLUSIONS

The relationship of auricular fibrillation to the course of rheumatic heart disease has been discussed. It has been pointed out that in order to study this phenomenon it is essential that the life histories of a large number of patients with rheumatic heart disease, who are studied until death, be analyzed and that a group with auricular fibrillation be compared with one in which it did not occur.

Of 644 such patients 42.8 per cent developed auricular fibrillation. It occurred with about equal frequency among males and females.

The most important conclusion to be drawn is that auricular fibrillation per se does not determine prognosis or life expectancy. It has been demonstrated in a number of ways that auricular fibrillation is usually a late manifestation in rheumatic heart disease and that it is most commonly observed in the relatively long standing cases. The die has already been cast when auricular fibrillation sets in.

There is no correlation between the age when patients first acquire rheumatic fever and the subsequent devolepment of auricular fibrillation; children who are afflicted with rheumatic fever in the first decade of life are just as likely to develop this arrhythmia as are patients first affected in later decades, provided they live long enough. The longer the disease lasts, the greater are the chances that patients will develop the irregularity. This being the case, it is but natural that the average duration of life is short once auricular fibrillation is established.

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THE INTERRELATIONSHIP OF ARTERIOSCLEROTIC HEART DISEASE AND CHRONIC CONGESTIVE FAILURE*

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THE clinical aspects of the acute and subacute phases of coronary artery disease are well established in modern medical literature. Studies on the chronic phase are less numerous. The picture of circulatory insufficiency occurring with coronary artery disease was known to the early writers on the subject as indicated by Leyden's[1] complete description of the clinical entity in 1884 and the somewhat later contributions of Obratzow and Straschesko.[2]

In following a large number of cases of arteriosclerotic heart disease, we were impressed by the fact that the outstanding symptoms and signs divide the material into two well-defined groups. One group consists of cases in which congestive failure, either early or late, is a characteristic phenomenon. The other group comprises patients who have recurrent seizures of angina pectoris for several years but do not develop congestive failure during the entire course of their disease. It was our purpose to determine whether there were common characteristics for each group which may make this division understandable.

The clinical records of 100 cases of chronic coronary artery disease and myocardial fibrosis, observed over a long period of time and proved by autopsy, were reviewed. Pulmonary congestion, enlargement of the liver, paroxysmal nocturnal dyspnea, manifest or latent edema were regarded as criteria of chronic congestive failure. No attempt was made to differentiate sharply between signs attributable to failure of the left or of the right ventricle. As we were dealing with the chronic forms of circulatory failure, more than temporary preponderance of one type over another could not be determined in the majority of instances.[3]

Among the 100 patients, 89 had definite evidence of congestive failure while 11 showed none of the above mentioned criteria. In the following discussion, the patients who were in, or gave a history of, congestive failure constitute Group A and those who had neither history nor signs of failure, Group B.

Vessel and muscle damage were common to both groups. In an attempt to evaluate their significance, we graded damage as slight, moderate, or severe. In Group A all types and extents of muscle damage from slight to severe were encountered, though those with severe dam-

*From the Medical Division of the Montefiore Hospital, service of Dr. L. Lichtwitz.

age predominated. Analysis of Group B showed moderate or severe damage in 8 out of a total of 11 cases and slight damage in 3. It follows from this observation that extensive destruction of heart tissue per se does not necessarily lead to chronic congestive failure and cannot be regarded, therefore, as the dividing factor between the two groups.

Attempts to correlate the duration or severity of congestive failure with the extent of damage to the heart were not successful. A long history of grave failure was found with relatively slight damage, while severe damage occurred with both short and long duration of failure.

The significance of age was next considered. In Group A the age limits of the cases with severe damage were found to be the widest, ranging from forty to seventy-nine years, approximately two-thirds being under sixty-five years. The age limits of Group B were more limited. With the exception of one man who was under sixty-two years, all were above sixty-five, the oldest being ninety-six years. It seems that chronic congestive failure may terminate the course of chronic coronary artery disease at any period of life. The greater longevity of Group B is striking. As it has been shown that the incidence of coronary artery thrombosis decreases in the seventh decade,[4] it can be presumed that the majority of the patients forming Group B had had their myocardial damage for a long time. Long duration of myocardial damage fails to explain the development of chronic congestive failure in the one group and its absence in the other.

The preponderance of enlarged hearts in the cases in failure and the absence of cardiac enlargement in those not in failure is immediately apparent. The term "cardiac enlargement" is used to indicate increase in muscle mass. It was impossible to relate heart weight to other body measurements because many of the patients were emaciated and others had fluid retention amounting to as much as 30 per cent of their total body weight. In order to avoid controversial discussion, we accepted 400 grams as the upper limit of the weight of the normal heart.[5] A liberal margin has to be allotted for normal fluctuations. In borderline cases hypertrophy of the muscle fibers when seen in at least two slides of tissue taken from different parts of the heart, was accepted as final evidence of increase in mass. The isolated, patchy hypertrophy frequently seen adjacent to infarcted areas was not considered as evidence of generalized hypertrophy.

Applying the criterion of heart weight, we found that in Group B the weight of only 2 of the 11 hearts exceeded 400 grams and 2 others showed microscopic generalized hypertrophy. The 4 patients with slight cardiac hypertrophy were bedridden for a long time because of complicating diseases, and the conditions favoring the development of cardiac insufficiency were absent. Some of the patients died of

recurrent acute coronary episodes. It seems that the common characteristic of Group B is the absence of chronic congestive failure and of significant cardiac hypertrophy.

In Group A cardiac hypertrophy was present in 84 of the 89 cases. There were 78 hearts weighing over 400 grams, the great majority between 500 and 800 grams. In 8 cases the heart weighed less than 400 grams but showed generalized muscle fiber hypertrophy microscopically. There were only 3 in this group in which cardiac hypertrophy could not be demonstrated either grossly or microscopically. In the overwhelming majority chronic congestive failure developed in the presence of cardiac hypertrophy. Both hypertrophy and failure of the right ventricle were present in a large number of cases in which damage from coronary artery disease was confined to the left ventricle. Right heart failure occurring with partial destruction of the left ventricle only, is a purely functional phenomenon. The fatty infiltration of the myocardium of the right ventricle which appears in some instances, is evidence of the anoxemia of failure and is not a primary muscle disease. (Table I.)

TABLE I

Total number of cases of chronic coronary artery disease and myocardial fibrosis	100
Group A—in failure	89
Group B—not in failure	11
I. Analysis of Group A. Total number of cases	89
1. Hypertrophied hearts	
(1) Heart weight in excess of 400 grams; gross hypertrophy	78
(2) Heart weight less than 400 grams; generalized microscopic hypertrophy of muscle fibers present	8
2. Nonhypertrophied hearts; heart weights less than 400 grams; generalized fiber hypertrophy absent	3
II. Analysis of Group B. Total number of cases	11
1. Cardiac hypertrophy	
(1) Heart weight in excess of 400 grams; gross hypertrophy	2
(2) Heart weight less than 400 grams; generalized microscopic hypertrophy of muscle fibers present	2
2. Nonhypertrophied hearts; heart weight less than 400 grams; generalized fiber hypertrophy absent	7

Analysis of material showing: (A) division of cases into a group with and a group without chronic congestive failure; (B) the relationship of cardiac hypertrophy to chronic congestive failure.

Comparison of our material with that from a general hospital where a large percentage of patients is admitted in the acute phases of coronary disease reveals interesting data. Nathanson[6] studied 113 cases of proved coronary artery disease including a large proportion in the acute stage. His figures show that the vast majority in congestive failure have definite cardiac enlargement. The material comprises a considerable number that have no cardiac enlargement. The inclusion of this group of small hearts in his study, 42 as compared with our 11,

resulted in augmenting his series of those not in failure, corresponding to our Group B. The proportion of his patients in failure without increase in muscle mass is, however, almost identical with ours, as there were only three instances of congestive failure with hearts weighing less than 400 grams. One of these hearts weighed 395 grams. It is questionable whether a heart weighing so close to the upper limit of normal can be safely regarded as not hypertrophied without considering the microscopic findings. Both his and our figures show that while congestive failure may develop without cardiac hypertrophy, this number is small both in absolute figures and by comparison.

It is apparent that patients suffering from arteriosclerotic heart disease fall into one group with, and another without, congestive failure. This division, with few exceptions, depends on the presence of cardiac hypertrophy in the first and its absence in the second group. *Chronic congestive heart failure in chronic arteriosclerotic heart disease is overwhelmingly the failure of the hypertrophied heart.*

For a better understanding of the foregoing observations we have to consider the rôle of chronic coronary artery disease itself, or the resulting myocardial weakness, in the development of cardiac hypertrophy. Localized, patchy hypertrophy is known to occur in infarcted areas. In recent reviews by pathologists[7] generalized cardiac hypertrophy is not given as one of the changes following interference with the coronary circulation and replacement fibrosis. That advanced coronary disease is not necessarily associated with cardiac hypertrophy was shown by Miller and Weiss,[8] Levine[9] and others.

It is difficult to evaluate cause and effect from a purely clinical study, because of the common coincidence of hypertension with coronary artery disease and the frequent, persistent drop in blood pressure following coronary thrombosis. It has been our experience that the statement of the patient that he never had had hypertension was frequently contradicted by the data of previous admissions of the same individual to other institutions. For this reason, the conclusion of Smith and Bartels[10] that cardiac hypertrophy is frequently due to coronary disease alone, because in their cases a history of previous high blood pressure was not obtained, does not seem valid. In another study of two cases,[11] these authors cite an instance of a previously normal-sized heart which, during the course of congestive failure associated with advanced coronary artery disease, became markedly enlarged. The paucity of similar case records militates against the plausibility of such a mechanism of cardiac enlargement. This objection holds true especially when the marked hypertrophy of hearts weighing 500 to 600 grams and more is ascribed solely to vessel damage. Since in the majority of these instances the heart is found already enlarged at the time coronary disease is discovered, it would be necessary to study

a series of patients whose previous histories including blood pressure figures and heart size are known before the onset of coronary disease. Such a study is needed in view of the incomplete and contradictory data in the literature on this problem.

Significant information on the problem whether coronary artery disease without hypertension can cause cardiac hypertrophy may be obtained from a study of cases of congenital anomalies of the coronary circulation. In addition to extensive myocardial fibrosis, generalized cardiac hypertrophy was found by Bland, White, and Garland[12] in the necropsy examination of an instance of anomalous origin of the left coronary artery from the pulmonary artery. The authors quote similar observations from the literature.

In experimental ligation of the coronary arteries in dogs Smith[13] found that hypertrophy of the right ventricle followed ligation of the right coronary artery. These results were contradicted by the recent experiments of Sutton and Davis[14] who showed by serial x-ray pictures and post-mortem studies of the heart, that experimental coronary occlusion and myocardial fibrosis do not lead to generalized cardiac hypertrophy in animals even when they are subjected to strenuous exercise, though localized aneurysms of the ventricle developed under such conditions.

Damage to the heart, other than that due to diminution of the blood supply, has been shown to cause cardiac hypertrophy in cases of acute and chronic myocarditis.[15, 16] Rheumatic carditis without valvular disease has also been known to lead to hypertrophied hearts.[17] The cases of so-called idiopathic cardiac hypertrophy were shown to be invariably associated with myocardial damage.[18] Cardiac enlargement, predominantly dilatation, has been observed clinically[19] and hypertrophy has been demonstrated experimentally in anemia.[20] It is apparent that the conditions for the development of cardiac hypertrophy are still present even when the blood supply to the heart is diminished or the heart muscle proper is the seat of extensive disease not caused by impaired myocardial circulation.

The pathological conditions discussed here have in common the diminution of contractile power of the heart. The question arises as to how this diminution in the contractility of the heart muscle fibers can lead to generalized hypertrophy. The adequate stimulus for hypertrophy of the fibers is the increased initial tension to which the muscle fiber is subjected irrespective of whether the work accomplished is increased or not. The sharp differentiation between increased work and increased tension in the genesis of cardiac hypertrophy as restated recently by Bohnenkamp[21] is of great importance for a proper understanding of the problem. There are many abnormal conditions in which, though the muscle fibers are subjected to increased ten-

sion, the work accomplished as measured by the criteria of work accepted in physics is not increased. This contention is best exemplified by acute myocarditis during which cardiac hypertrophy develops at a time when clinical signs of cardiac inefficiency appear because of the diminution of fiber contractile power. The development of cardiac hypertrophy in the presence of definitely diminished cardiac efficiency can thus be explained.

Fiber contraction with increased initial tension leads at least temporarily to greater force of systolic ejection.[22, 23] The increased initial fiber tension is brought about by incomplete relaxation of the fibers during diastole. The increased force is needed to overcome resistance in the path of the expelled blood stream as exemplified by hypertension, aortic or pulmonic ostial disease. Compensation for primary loss of contractile power of the fibers caused by intrinsic myocardial disease is also made possible by increased initial fiber tension. The first result of increased resistance, or of primary diminution of contractile power, is incomplete systolic emptying of the ventricle followed by increased diastolic volume. The increased diastolic filling accentuates the processes discussed above. In the hypertrophy of the anatomically and functionally impaired heart lies the mechanism which may eventually lead to failure without the necessity of additional damage. With the persistence of the increased fiber tension a point is reached sooner or later at which the height of the increased fiber tension is not met by an equivalent increase in fiber contraction.[22] At this stage, a vicious cycle may develop. While the "work" of the heart actually performed is decreased, the additionally increased tension to which the fibers are subjected still may cause further hypertrophy and improved function temporarily. The result of this process, however, is increasing inefficiency of systolic contraction leading eventually to increased intraventricular, then intra-auricular and finally increased venous tension and to the clinical picture of stasis.[23]

Whether lessened fiber contractile power resulting from chronic coronary artery disease or increased peripheral resistance is the primary stimulus for the augmented fiber tension with which the heart has to work, failure with few exceptions is the end-state of cardiac hypertrophy. These few exceptions are the small number of cases in our own and Nathanson's series and those of others in the literature[1] in which chronic congestive failure with advanced coronary artery disease was associated with atrophied, previously nonhypertrophied hearts. The factors that prevent fiber hypertrophy in response to the undoubtedly existing increased initial fiber tension in these nonhypertrophied hearts in failure are still unknown. The ultimate cause of failure of these hearts is identical with that of the hypertrophied hearts.

Myocardial fibrosis of coronary disease could, from a physiological point of view, be considered adequate cause for the development of

cardiac hypertrophy. This opinion is also held by White.[24] Our observations and those in the literature are, however, so contradictory on this point that we find it difficult to accept this view without further study. Hypertension, present or antecedent, was in our opinion the cause of cardiac hypertrophy in the majority of our cases. In the absence of definitely elevated blood pressure figures, we attributed, as did Bell and Clawson,[25] left ventricular hypertrophy, when found without a valvular lesion or renal disease, to antecedent hypertension. Several patients who had small hearts with severe long standing hypertension were not in failure. It seems that circulatory failure developed when hypertension was associated with hypertrophied hearts. The fact that cardiac hypertrophy was present in the cases showing circulatory failure is more important than the factors leading to cardiac hypertrophy. The rôle of chronic coronary artery disease is twofold: (1) diminution of the blood supply of the hypertrophied heart necessarily accelerates the development of myocardial insufficiency; (2) myocardial fibrosis, by lessening the contractility of the muscle fibers, may lead to increased fiber tension and be the cause of cardiac hypertrophy.

The foregoing observations may have some prognostic significance. Patients who have hypertrophied hearts with coronary artery disease are more likely to develop congestive failure than those with non-hypertrophied hearts. This fact should be considered in prognosticating the future of an individual who has survived myocardial infarction.

Hypertrophy of the heart muscle cannot be considered the ultimate cause of failure. It seems, however, the only and, we believe, the most important common characteristic of the group of cases in chronic congestive failure. Hypertrophy is only an indication that the heart has for a long time worked under increased fiber tension. The failure of the hypertrophied heart to maintain the force of systolic ejection cannot be explained from a purely anatomical concept. That structural damage is not the sole cause of myocardial insufficiency was stated long ago in a fundamental contribution by Aschoff.[26] For an understanding of the factors concerned in the development of congestive failure, it is necessary to study the metabolism of muscle function. Such an approach to the problem was recently made by Cowan[27] and by Seecof, Linegar and Myers.[28]

SUMMARY

It was the purpose of this study to determine what factors are responsible for the development of chronic congestive failure in chronic coronary disease and myocardial fibrosis.

The clinical and post-mortem records of 100 unselected cases were studied. The overwhelming majority were in, or gave a history of, congestive failure. Varying degrees of vascular and myocardial dam-

TABLE II

TABULATION OF THE MATERIAL ACCORDING TO AGE, SEX, HEART WEIGHT, AND PRESENCE OR ABSENCE OF CHRONIC CONGESTIVE FAILURE*

CASE	PATIENT	AGE IN YEARS	SEX	HEART WEIGHT IN GRAMS	CHRONIC CONGESTIVE FAILURE	
1	B. M.	67	M.	550	Present	
2	M. G.	48	M.	600	Present	
3	M. G.	76	M.	680	Present	
4	A. S.	50	M.	400	Present	Hypertrophy
5	R. R.	55	M.	490	Present	
6	S. O.	65	M.	650	Present	
7	M. S.	64	M.	600	Present	
8	S. P.	66	F.	570	Present	
9	A. S. K.	65	M.	600	Present	
10	A. S.	68	M.	520	Present	
11	B. U.	73	F.	500	Present	
12	T. P.	58	F.	360	Present	Hypertrophy
13	I. B.	63	F.	340	Present	Hypertrophy
14	G. S.	73	M.	490	Present	
15	A. B.	54	F.	600	Present	
16	L. C.	53	M.	480	Present	
17	A. S.	56	M.	400	Present	Hypertrophy
18	E. G.	68	F.	380	Present	Hypertrophy
19	D. R.	59	M.	850	Present	
20	M. G.	60	M.	500	Present	
21	S. F.	54	M.	900	Present	
22	R. R.	60	F.	700	Present	
23	D. C.	71	F.	430	Present	
24	S. R.	53	M.	680	Present	
25	J. G.	57	M.	610	Present	
26	T. M.	78	F.	380	Present	Hypertrophy
27	B. N.	38	F.	600	Present	
28	B. H.	73	M.	700	Present	
29	J. S.	52	M.	900	Present	
30	G. S.	56	M.	450	Present	
31	H. B.	65	M.	500	Present	
32	G. N.	64	M.	550	Present	
33	M. K.	54	M.	500	Present	
34	N. F.	60	M.	480	Present	
35	J. M.	63	M.	530	Present	
36	I. R.	49	M.	600	Present	
37	H. R.	56	M.	500	Present	
38	A. P.	65	M.	650	Present	
39	D. R.	71	M.	250	Present	No hypertrophy
40	H. S.	54	M.	550	Present	
41	S. N.	75	F.	530	Present	
42	L. T.	62	M.	620	Present	
43	E. D.	65	F.	540	Present	
44	Y. S.	59	F.	380	Present	Hypertrophy
45	M. H.	62	M.	300	Absent	No hypertrophy
46	A. J.	75	M.	500	Absent	
47	J. H.	56	M.	510	Absent	
48	J. G.	64	M.	800	Present	
49	M. G.	54	M.	700	Present	
50	H. F.	54	M.	800	Present	
51	A. H.	57	M.	600	Present	
52	S. T.	72	M.	550	Present	
53	K. S.	70	F.	270	Absent	No hypertrophy
54	J. J.	68	M.	280	Absent	No hypertrophy

*Hearts weighing less than 400 grams or showing no gross hypertrophy were examined microscopically for generalized fiber hypertrophy and the results noted.

TABLE II—CONT'D

CASE	PATIENT	AGE IN YEARS	SEX	HEART WEIGHT IN GRAMS	CHRONIC CONGESTIVE FAILURE	
55	N. K.	65	M.	300	Present	Hypertrophy
56	A. C.	67	M.	380	Absent	No hypertrophy
57	M. L.	75	M.	300	Absent	No hypertrophy
58	M. T.	53	M.	600	Present	
59	M. A.	59	M.	650	Present	
60	R. O.	65	F.	400	Present	Hypertrophy
61	D. B.	71	F.	600	Present	
62	M. W.	62	M.	680	Present	
63	M. G.	64	M.	700	Present	
64	A. S.	96	F.	300	Absent	Hypertrophy
65	H. S.	75	F.	350	Present	
66	M. M.	46	M.	620	Present	
67	T. B.	63	M.	600	Present	
68	S. R.	61	F.	360	Present	Hypertrophy
69	G. L.	68	M.	260	Absent	No hypertrophy
70	W. P. N.	67	M.	500	Present	
71	M. S.	62	M.	525	Present	
72	B. B.	59	F.	500	Present	
73	A. S.	79	F.	415	Present	
74	L. T.	62	F.	620	Present	
75	S. R.	60	M.	400	Present	Hypertrophy
76	L. P.	60	M.	500	Present	
77	S. B.	66	M.	450	Present	
78	B. G.	64	M.	550	Present	
79	P. P.	57	F.	450	Present	
80	L. L.	79	M.	300	Absent	No hypertrophy
81	B. P.	62	F.	680	Present	
82	A. E.	69	M.	420	Present	
83	A. C.	83	F.	470	Present	
84	G. C.	86	M.	350	Absent	No hypertrophy
85	G. F.	62	M.	410	Present	
86	M. C.	67	F.	500	Present	
87	A. S.	78	M.	800	Present	
88	N. W.	54	M.	480	Present	
89	L. C.	40	M.	450	Present	
90	L. K.	62	M.	620	Present	
91	L. W.	60	M.	800	Present	
92	H. K.	63	M.	600	Present	
93	W. M.	68	M.	620	Present	
94	J. S.	65	M.	550	Present	
95	H. G.	64	M.	500	Present	
96	F. T.	61	M.	350	Present	Hypertrophy
97	E. D.	55	M.	700	Present	
98	R. S.	45	F.	500	Present	
99	M. S.	69	F.	250	Present	No hypertrophy
100	A. P.	57	M.	755	Present	

age were common to the entire series, but the vast majority of those in congestive failure had definite and in most instances advanced cardiac hypertrophy. There were but three exceptions to this rule. The group not in failure had nonhypertrophied or, in a few cases, slightly hypertrophied hearts.

The characteristic feature of the chronic congestive phase of chronic coronary artery disease is the presence of cardiac hypertrophy.

The genesis of cardiac hypertrophy in relation to muscle damage is discussed. The view is accepted that increased initial fiber tension rather than increased work is the stimulus for generalized cardiac hypertrophy. Contraction with increased initial tension compensates for inadequate contractility. Myocardial disease by diminishing contractile power calls forth increased initial fiber tension and may, according to the above theory, be the cause of generalized cardiac hypertrophy. Application of this concept to the question of cardiac hypertrophy in coronary artery disease is not sufficiently supported, however, by clinical experience. Since the data in the literature are contradictory on this point, it is necessary to study further the causal relationship of chronic coronary artery disease to generalized cardiac hypertrophy by following patients whose blood pressure figures and heart size are known before and after the onset of the disease. Our present belief is that in the majority of cases generalized and advanced cardiac hypertrophy is caused by hypertension, present or antecedent, and not by vascular and myocardial damage.

Diminished blood supply and severe muscle damage produce loss of contractility and may cause failure without leading to fiber hypertrophy. The striking predominance of hypertrophied hearts of the group in failure, however, indicates that it is work under long standing increased fiber tension irrespective of the cause, and the eventual loss of contractile power of the hypertrophied fiber, that leads to chronic congestive failure.

Congestive failure in chronic arteriosclerotic heart disease is—like that of other types of heart disease—overwhelmingly the failure of the hypertrophied heart. (Table II.)

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THE VALUE OF SOUND RECORDS IN THE DIAGNOSIS OF MITRAL STENOSIS*

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EINTHOVEN,[1] Battaerd,[2] Lewis,[3] and others made use of the string galvanometer to record heart sounds soon after this instrument began to be employed in the study of heart disease. These early studies brought out many interesting and useful facts regarding time relations of heart sounds and heart murmurs. Since they were carried out, great strides in the technic of sound recording have been made, and the development of the vacuum-tube amplifier and microphones of the condenser and of the electromagnetic type have placed at our disposal methods far superior to those formerly in use. In this country, however, comparatively few investigators have employed these methods to make graphic records of heart sounds. The work of Wolferth and his collaborators,[4, 5] of Asher,[6] of Parsonnet and Hyman,[7] and of Hirschfelder[8] should be mentioned. Abroad, they have been used by Posener and Trendelenburg,[9] Pieraeh,[10] Bass,[11] Jaenisch and Weber,[12] Groedel,[13] and others. In the last two articles mentioned, it is pointed out that sound records may be of considerable diagnostic value. In this laboratory records of heart sounds and murmurs have been taken for a number of years, and we have found them often of value, particularly when the heart rate is rapid or when, for other reasons, the sounds heard on auscultation are difficult to interpret. It is the purpose of this article to show that graphic records of the sounds heard at the cardiac apex are particularly useful in the diagnosis of mitral stenosis.

It very frequently happens that, although the presence of mitral stenosis is strongly suspected, no distinct apical diastolic murmur can be heard, and the diagnosis remains in doubt. As an illustration, let us consider a hypothetical case: a young man gives a history of typical rheumatic fever and displays on physical examination several or all of the following physical signs—slight or questionable enlargement of the heart, a snapping mitral first sound, an accentuated pulmonic second sound, a moderately sharp systolic blow at the apex. The fluoroscopical examination shows slight prominence of the upper left border of the cardiac silhouette or slight narrowing of the retrocardiac space in its mid-

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dle third. The electrocardiogram is not definitely outside normal limits. With these findings a tentative diagnosis of mitral stenosis is justified, but the presence of this lesion is not certain until an apical diastolic murmur has been demonstrated. In several cases of this kind which have recently come under observation, graphic records of the apical sounds have clearly revealed a diastolic murmur which several competent observers had failed to detect by auscultation.

METHODS

Two Einthoven galvanometers arranged to record simultaneously on the same film were employed for all sound registration work. One in-

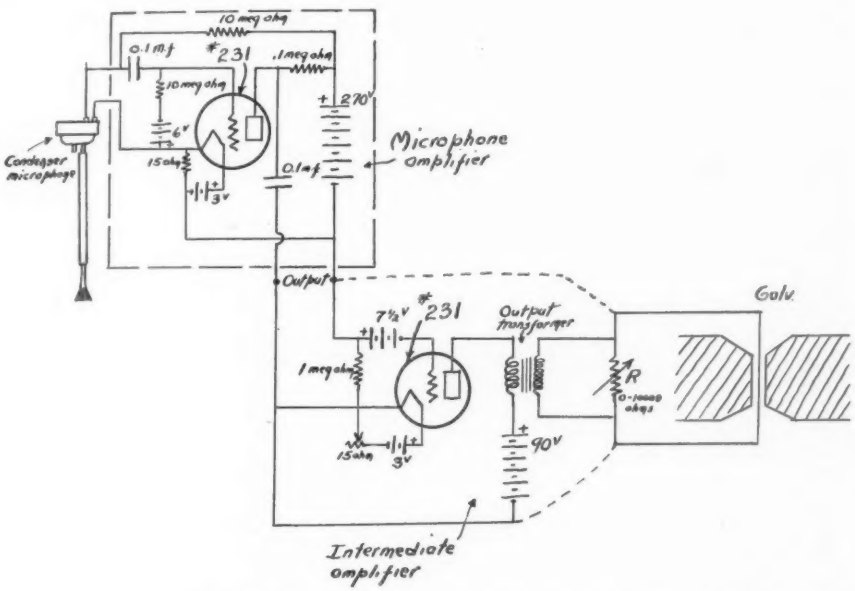

Fig. 1.—Diagram showing the circuit employed with the condenser microphone and the connections to the string galvanometer (see text).

strument was used to record one of the standard electrocardiographic leads, usually Lead I, and the other to take the sound tracing. The arrangement of the condenser microphone and its connections with the string galvanometer are shown in Fig. 1. The heart sounds were conveyed to the microphone through a stethoscope end-piece attached to a flexible rubber tube about 45 cm. long. The inside diameter of this tube was 4 mm. When the sounds to be recorded were unusually loud the output terminals of the microphone amplifier were connected directly to the galvanometer as shown by the dotted lines in Fig. 1. In the great majority of cases, however, a second stage of amplification was necessary in order to obtain tracings of suitable amplitude. In Fig. 1

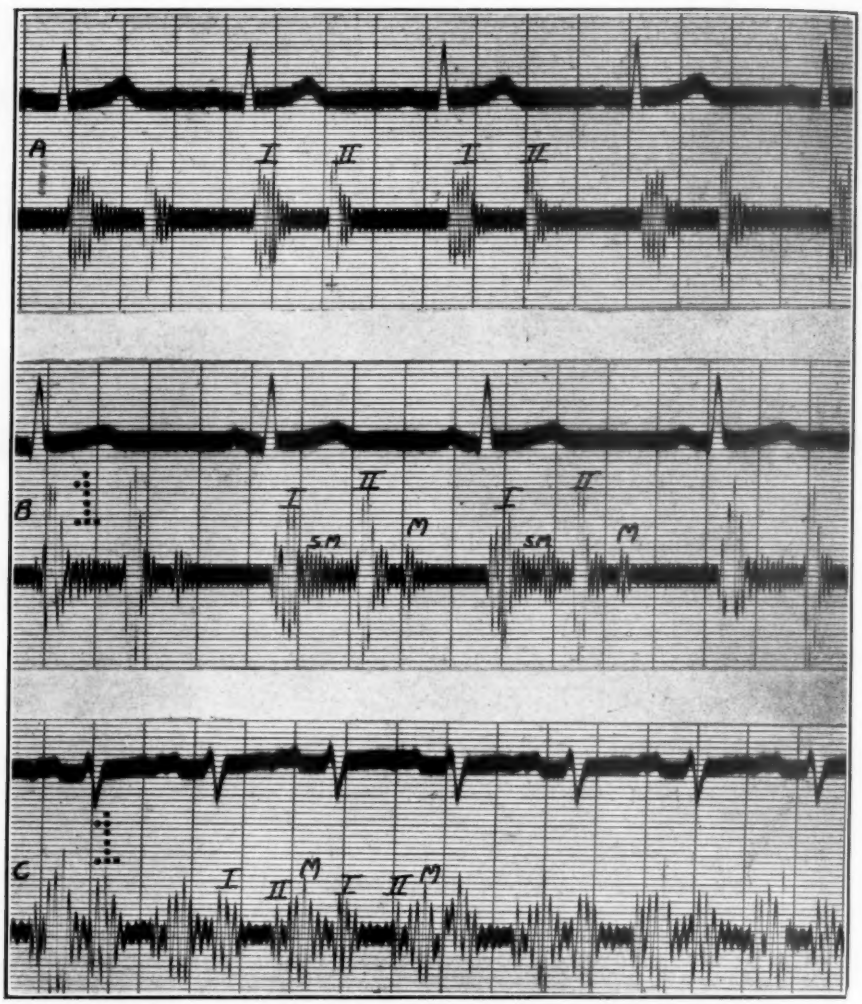

Fig. 2.—The upper curve, in each case, is standard Lead I of the electrocardiogram, and the lower curve, a record of the apical heart sounds. *A*, Curves from a subject with a normal heart; *B*, curves from Case 1; *C*, curves from Case 2.

The heart sounds and murmurs are labelled as follows: *I*, first heart sound; *II*, second heart sound; *M*, diastolic murmur; *S.M.*, systolic murmur. Interval between time lines = 0.2 second.

the second vacuum tube and the associated circuits are labelled "intermediate amplifier."*

*It should be pointed out that the appearance of a sound tracing obtained at a given point in the precordium varies with the type of stethoscope end-piece employed and with the nature of the electrical circuit used. The most satisfactory records of high-pitched murmurs are obtained by using a large Bowles stethoscope (with the diaphragm in place) and by employing a series condenser with a capacitance of 0.001 microfarad or less in the galvanometer circuit. These arrangements tend to make the sound components of higher frequency more prominent in the record. In the present study we were primarily interested in the registration of murmurs of low pitch. For that reason a stethoscope end-piece of the bell type was used and no series condenser of small capacitance was employed. Some of the tracings obtained give, therefore, an inadequate picture of the sounds heard on auscultation. A high-pitched systolic murmur, for example, which was fairly loud to the ear may be scarcely visible in the sound tracing.

To prevent an excessive current from passing through and destroying the galvanometer string, a variable resistance, R, was placed in parallel with it. By regulating this resistance, the current through the string could be brought to the desired value. A tracing of the apical heart sounds of a normal subject taken by the method outlined is reproduced in Fig. 2*A*. This record may be compared with the abnormal tracings, described later, which were taken in exactly the same manner.

OBSERVATIONS

CASE 1.—The first patient was a boy, eighteen years old, who had been in good health until February, 1934, when he became acutely ill with fever and swollen, painful joints. The knees, ankles, elbows, wrists, and hips were involved in turn. These symptoms persisted for several weeks. After they had disappeared, there was dyspnea on exertion, and it was this symptom which brought the patient to the hospital in August, 1934. Physical examination of the heart at this time showed no definite enlargement. The heart rate was 80 per minute, and the rhythm was normal. At the apex, the first sound was loud, and a rather harsh systolic murmur was heard. Some observers noticed in early diastole a sound not unlike an unusually prominent normal third heart sound. Nothing else could be made out even when the patient was examined in the left lateral position after exercise. The pulmonic second sound was accentuated and, at times, widely split. The systolic blood pressure was 110 mm. Hg; the diastolic, 70 mm. Hg. There were no signs of cardiac failure. An orthodiagram showed slight fullness of the left cardiac border, but no definite enlargement of the heart. A diagnosis of mitral stenosis was not made until the sound tracing shown in Fig. 2*B* demonstrated the presence of a short, early diastolic murmur. In some cycles the vibrations representing this sound extended over an interval of 0.1 second. Its duration was, therefore, too great to permit us to consider it either a physiological third heart sound or a protodiastolic gallop sound.

CASE 2.—The second patient, also a youth of eighteen years, had always been fairly well until early in April, 1934, when he began to notice "fluttering" of the heart, substernal oppression, and dyspnea on exertion. He became so nervous at times that he had difficulty in writing. In spite of these symptoms he continued to attend school and to engage in athletic sports. About three months after the beginning of his illness, he consulted a physician who advised rest in bed and prescribed Lugol's solution. Late in July, 1934, he was admitted to a small hospital for thyroidectomy, but because of persistent cardiac pain this operation was not performed. He first came to the University Hospital early in August, 1934. Aside from frequent upper respiratory infections and an attack of severe streptococcus sore throat the past history was essentially negative. He had never had rheumatic fever or chorea. Physical examination showed gross cardiac enlargement with the left border of cardiac dullness at the left anterior axillary line. The heart was very overactive, and the average heart rate was 125 per minute. The rhythm was normal except for an occasional extrasystole. The heart sounds were very confusing and difficult to interpret. At the apex there was a soft blowing murmur, presumably systolic in time, while just inside the apex two fairly loud low-pitched sounds, difficult to place in the cardiac cycle, were heard. The systolic blood pressure was 102, the diastolic 80 mm. Hg. The lungs were clear, and there were no signs of cardiac failure. An orthodiagram showed a frontal plane area 79 per cent in excess of that predicted by the Hodges-Eyster formula, nearly complete obliteration of the retrocardiac space, and slight fullness of the left cardiac border. The electrocardiogram

revealed pronounced right axis deviation and large P deflections, a combination rarely seen except in advanced mitral stenosis. The basal metabolic rate was minus 5 per cent. A sound tracing (Fig. 2*C*) taken from a point inside the apex beat explained the peculiar physical findings and made possible a positive diagnosis of mitral stenosis. It will be seen that a prominent murmur occupies the greater part of diastole. It reaches its maximum amplitude in the tracing about 0.1 second after the end of the second sound, and there is no suggestion of presystolic accentuation. The first sound is represented by vibrations of considerable size, whereas the vibrations of the second sound are insignificant. Systole is quiet.

CASE 3.—The third patient was a married woman, aged twenty-three years, who had her initial attack of rheumatic fever at the age of twelve years. This illness was followed by dyspnea on exertion, palpitation, and occasional precordial pain. Recently there had been slight swelling of the ankles. Three weeks prior to admission to the hospital she again developed fever and joint symptoms, which were still present in October, 1933, when she was first seen. Examination showed the heart to be greatly enlarged with the left border of cardiac dullness nearly in the anterior axillary line. The cardiac rhythm was normal, and the rate was approximately 100 per minute. At the apex a definite systolic thrill was felt, and a loud harsh systolic murmur was heard on auscultation. Regarding the presence of a mitral diastolic murmur, the opinion of the various observers differed greatly. Some thought they could hear a presystolic murmur; others denied the existence of such a murmur; and still others were uncertain whether it was present or not. No evidence of an aortic lesion was found. The systolic blood pressure was 110, the diastolic 55 mm. Hg. The lungs were clear, and there were no signs of congestive cardiac failure other than slight pitting edema of the ankles. An orthodiagram showed a frontal plane area 72 per cent larger than that predicted by the Hodges-Eyster formula. The shape of the cardiac silhouette suggested preponderant enlargement of the left ventricle. The electrocardiogram showed a P-R interval measuring 0.23 second, large P deflections, and a QRS interval of approximately 0.1 second, suggesting the presence of a slight defect in intraventricular conduction. There was no axis deviation. Two apical sound records were made. The first (Fig. 3*A*) was taken with the patient in the supine position and shows the systolic but no definite diastolic murmur.* The second (Fig. 3*B*) was taken with the patient in the left lateral position and immediately after the inhalation of amyl nitrite. It shows a definite presystolic murmur.

CASE 4.—The last patient was a girl, aged thirteen years, who had been in good health until eleven weeks prior to her admission to the hospital. Her illness began with stiffness of the neck, headache, slight fever, and attacks of vomiting. These symptoms were followed by a migratory polyarthritis, characterized by swelling, tenderness, and slight redness of the joints. Practically all the larger joints except the hips were involved. The joint difficulties lasted for several weeks; they had hardly subsided when the patient began to have choreiform movements, which were still present when she came to the hospital in August, 1934. There was no history of a previous attack of rheumatic fever, but the patient had had sore throat with fever frequently, prior to removal of the tonsils about a year before. In early childhood she had had measles, whooping cough, and scarlet fever, all without complications. Physical examination showed no definite enlargement of the heart. The

*Low-pitched vibrations occurring about 0.2 second after the second sound are seen in this record (Fig. 3*A*). The heart rate was approximately 70 per minute when this tracing was taken, and it seems probable that under these circumstances the velocity of flow through the mitral valve was maximal in early diastole and that the vibrations mentioned represent an inaudible early diastolic murmur. With the shortening of diastole due to the increase in heart rate, these phenomena occur later in diastole and, in conjunction with the effects of auricular systole, produce the definite presystolic murmur seen in Fig. 3*B*.

left border of cardiac dullness was inside the nipple line. The heart rate was slightly over 100 per minute, and the rhythm was normal. At the apex the first sound was not unusually loud; a soft systolic blow was present. No apical diastolic murmur was heard by any of several examiners. At the base both an aortic systolic and an aortic diastolic murmur were noted. The pulmonic second sound was, perhaps, slightly accentuated. The systolic blood pressure was 130, the diastolic 70 mm. Hg. There were no signs of cardiac failure. An orthodiagram showed no cardiac enlargement, but the outline of the left cardiac border was reported as suggesting a

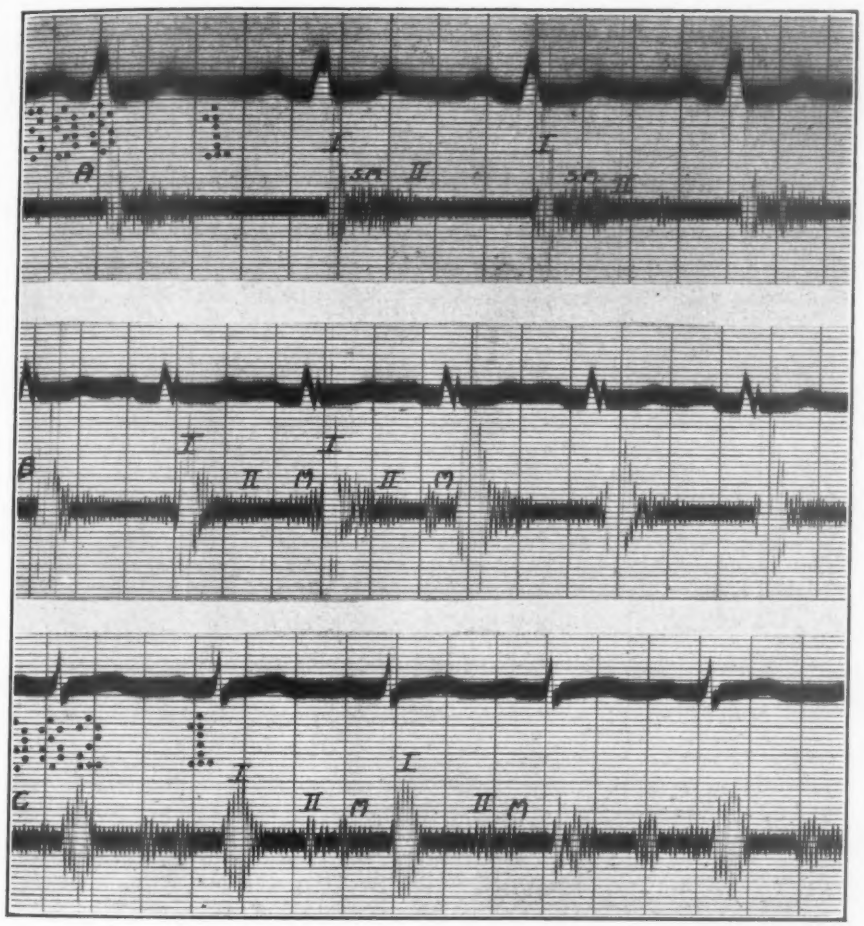

Fig. 3.—The upper curve, in each case, is standard Lead I of the electrocardiogram and the lower curve a record of the apical heart sounds. *A*, Curves from Case 3 with the patient in the supine position; *B*, curves from Case 3 with the patient in the left lateral position and after the inhalation of amyl nitrite; *C*, curves from Case 4.

The heart sounds and murmurs are labelled as follows: *I*, first heart sound; *II* second heart sound; *M*, diastolic murmur; *S.M.*, systolic murmur. Interval between time lines = 0.2 second.

mitral lesion. Aside from sinus tachycardia, the electrocardiogram was negative. On the basis of these findings a diagnosis of acute rheumatic infection with chorea and aortic insufficiency was made. The patient was referred to the Heart Station for examination at which time a definite but not loud early diastolic murmur was

heard at the apex. The suggestion that mitral stenosis should be included in the diagnosis was received with some scepticism by those in charge of the patient until the sound record shown in Fig. 3*C* was taken. It shows a low-pitched murmur which in most cycles is confined to early diastole.

DISCUSSION

It will be observed that three of the four patients presented had murmurs which were essentially early diastolic in time and showed no presystolic accentuation. It seems likely that murmurs of this kind are frequently overlooked. There are obvious reasons why this should often be the case. Most physicians have been taught that the characteristic murmur of mitral stenosis is presystolic and have not trained themselves to listen carefully for low-pitched sounds in early diastole. In the second place, sounds of this kind are difficult to hear. The presystolic murmur of mitral stenosis, even when it is faint and very low pitched, is apparently more easily recognized, possibly because it is usually associated with a loud snapping first sound and the combination of murmur and sound has a characteristic quality. It should be remembered that the human ear is much more sensitive to high-pitched sounds than to sounds of low frequency. The sound pressure, in dynes per square centimeter, that must be exerted in order to reach the threshold of audibility by a murmur with a frequency of fifty cycles per second is nearly one hundred times as great as that which must be exerted by a murmur with a frequency of two hundred cycles per second. The fundamental frequencies present in the murmurs of mitral stenosis are very low, somewhere in the neighborhood of fifty cycles per second, and the human ear is relatively insensitive to these sounds. It is also known that individuals differ greatly in their ability to hear low-pitched sounds and even more in their ability to hear faint sounds of this kind. It is, therefore, to be expected that a sound-recording system whose response does not decrease in the low-frequency range will often register low-pitched sounds that have escaped detection on auscultation. Battaerd[2] observed vibrations of low frequency at the beginning of the first sound in some of his normal subjects and pointed out that these vibrations were inaudible. We have frequently obtained excellent records of the physiological third heart sound and also of the auricular sounds in heart-block when these sounds were very difficult to hear or were inaudible. Our experience with sound tracings from patients with mitral stenosis indicates that, even with our present, rather imperfect set-up, murmurs that are heard with difficulty by most observers can be easily recorded. With further refinements in apparatus and technic it may be possible to record low-pitched sounds that are well below the limit of audibility.

The first and fourth patients presented were chosen as characteristic examples from a considerable number, all of whom displayed nearly in-

audible, early diastolic murmurs which were clearly depicted in the sound tracings. The great majority of patients with faint murmurs of this type probably have only slight stenosis of the mitral valve; nevertheless, the diagnosis of such lesions is of great importance. Even in the case of far advanced mitral stenosis, the methods usually employed may fail to yield data that permit the diagnosis of this valve lesion to be made with certainty. The second patient presented illustrates the difficulties that may arise. In this instance also the first clear evidence of the presence of this valve lesion was furnished by the sound tracing.

SUMMARY

For the purpose of illustrating the value of graphic records of the heart sounds in the diagnosis of mitral stenosis, four cases in which the only unequivocal evidence of the presence of this valve lesion was furnished by simultaneous tracings of the apical heart sounds and the electrocardiogram are presented.

Many patients with early mitral stenosis display low-pitched diastolic murmurs which show no presystolic accentuation and are often difficult to hear. The insensibility of the human ear to sounds of low frequency probably explains why many of these murmurs are missed on auscultation. The advantages which graphic methods possess in their detection are emphasized.

In some cases of well advanced mitral stenosis the apical heart sounds heard on auscultation are difficult to interpret, and in these cases also sound tracings are often of great diagnostic value.

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OCCLUSIVE DISEASES OF THE CORONARY ARTERIES*

An Analysis of the Pathological Anatomy in One Hundred Sixty-Eight Cases, With Electrocardiographic Correlation in Thirty-Six of These

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THERE have been many studies in recent years on the subject of coronary artery disease. However, as pointed out by Barnes and Ball,[1] relatively few contributions have dealt with the details of the pathological anatomy. Most of the studies were based on comparatively small series of cases. Furthermore, there have been very few reports on the correlation of electrocardiographic and necropsy findings.

In this paper no effort will be made to review the literature, as our object is to present mainly the pathological details that have been found in the study of a fairly large number of cases of occlusive diseases of the coronary arteries. Although the number of available electrocardiograms was comparatively small, nevertheless, we considered it worth while to correlate them with the post-mortem findings.

We have divided our cases into three main groups, as follows:

I. Atherosclerotic
II. Syphilitic
III. Miscellaneous.

I. *Atherosclerotic Group*

In this group the underlying pathological condition was sclerosis of the coronary arteries. Occlusion of a coronary vessel was caused either by a process of progressive stenosis and patchy calcification or by a superimposed thrombus. There were 150 cases in this group, of which 113 showed complete occlusion of one or more of the coronary arteries, while 37 had marked sclerosis and stenosis with almost complete occlusion of a vessel or branch. There were 78 instances of thrombosis of a vessel.

Sex.—One hundred twenty-five of the subjects in this group were men, and twenty-five were women. These figures would seem to indicate a marked preponderance of males. However, an allowance must be made for the larger number of male patients in Bellevue Hospital.

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Age.—The age was definitely given in 142 cases. Table I shows their distribution by decades of life. It will be noted that approximately 65 per cent of the occlusions had occurred among patients who were between the ages of fifty and sixty-nine years when they died. There were only three instances of occlusion in patients under forty years of age. Similar figures were given by Barnes and Ball.[1]

TABLE I

DISTRIBUTION OF CASES OF OCCLUSION OF THE CORONARY ARTERIES BY DECADES OF LIFE

AGE GROUPS	30-39	40-49	50-59	60-69	70-79	80-89
Number of cases	3	25	36	56	19	3

Weight of Heart.—In the majority of cases the weight of the heart was considerably above the average calculated weight for the sex and age of the patients. Table II shows the weight in ninety-four of the cases. In sixty-nine instances the weight was more than 400 gm. and in a little more than half of these subjects the weight exceeded 500 gm. However, in most of these instances of cardiac enlargement there was evidence of moderate or marked generalized arteriosclerosis with frequent involvement of the renal vessels. In many of these there was a clinical record of hypertension or evidence of the presence of hypertension prior to the occurrence of the coronary occlusion. In a few cases

TABLE II

GROUPING OF HEARTS IN 94 CASES OF CORONARY OCCLUSION BY WEIGHT IN GRAMS

WEIGHT IN GRAMS	200-300	301-400	401-500	501-600	601-700	701-800	801-900
Number of cases	4	21	17	19	23	7	3

there was also evidence of an aortic or mitral valvulitis or calcification of these valves. Chronic nephritis and adhesive pericarditis were observed in many instances. It is also to be noted that in twenty-five cases, some of which showed a very marked degree of sclerosis, the weight was within normal range. It would seem, therefore, that other factors besides the interference with the coronary circulation were mainly responsible for the cardiac hypertrophy in these cases.

Pericarditis.—Pericarditis was found in 50 of the 150 cases. Of these, 16 were instances of recent and 34, of old healed pericarditis. This is a higher incidence than that observed by other workers. It is quite possible that in a number of patients with old fibrous pericarditis the lesion was the sequel of an inflammatory process and not of myocardial infarction.

Site of Occlusion.—Complete occlusion of one or more vessels was demonstrated in 113 of the cases. As shown in Table III, the left coronary artery was found occluded in 100 instances; the main trunk

and its descending branch was involved in 92 cases, and the circumflex branch in 8 cases. Occlusion of the right coronary artery occurred in 29 cases. Sixteen of the 113 cases showed multiple occlusions, that is, involvement of more than one vessel or branch. It will be noted, therefore, that occlusion of the left coronary artery occurred about three times as frequently as that of the right. The anterior descending branch of the left coronary artery was the vessel predominantly involved. The designation of this branch as "the artery of death" would therefore seem appropriate. These findings are somewhat at variance with the reports of Parkinson and Bedford[2] and Barnes and Ball.[1] These authors, however, have based their studies on much smaller series of cases.

TABLE III

SITE OF OCCLUSION

ARTERY OR BRANCH OCCLUDED	LEFT CORONARY			RIGHT CORONARY	MULTIPLE
	MAIN TRUNK	DESCENDING BRANCH	CIRCUMFLEX BRANCH		
Number	7	85	8	29	16

As previously noted, there were 78 instances of coronary occlusion by a thrombus. Of these, 57 occurred in the left and 21 in the right coronary artery. Thrombosis of more than one vessel or branch occurred in 9 cases. In several instances there was an old thrombus in one vessel and a recent one in another vessel or branch. In two instances the occluded branch showed both an old organized and a fresh thrombus. These findings, as pointed out by De la Chapelle[3] and others, furnish direct evidence that coronary thrombosis in human beings is not always fatal.

Degree of Sclerosis in Coronary Arteries.—It has been observed by many workers that the coronary arteries are frequently the seat of atherosclerosis, involving mainly the larger and medium-sized vessels. Brooks,[4] in his study of the incidence of visceral arteriosclerosis as revealed by gross examination, found the coronary vessels second in the order of frequency of involvement. In his study of arteriolosclerosis, Fishberg[5] has pointed out that the larger vessels in the coronary system are frequently involved by atherosclerosis although the arterioles are implicated only to a minor degree. Wartman[6] found the incidence of coronary sclerosis to be 57.5 per cent in 405 hearts examined grossly, and 49.2 per cent in 346 hearts studied microscopically.

In our series the hearts were examined in the gross and occasionally microscopically also. With very few exceptions, the coronary arteries showed fairly marked sclerosis. In most instances the degree of sclerosis was about the same in the right and left coronary arteries. There were several instances of very marked sclerosis of the coronary vessels in

subjects who were between the ages of thirty-five and forty-five years when they died. In all of the cases in this group, therefore, coronary occlusion was a process secondary to coronary sclerosis.

Site of Infarction.—Infarction of the myocardium was recognized as either acute or old fibrous. Diffuse fibrosis was not grouped with the infarcts. Definite localization of infarcts was determined in 118 of the 150 cases. The presence of more than one infarct was noted in several instances. In the group of thirty-seven cases with marked coronary sclerosis and stenosis but without complete occlusion, a myocardial infarct was localized in twenty-four. Many of the cases with marked coronary sclerosis and with complete occlusion of one of the vessels showed only diffuse fibrosis of the myocardium. In three instances of acute coronary occlusion by a thrombus there was no evidence of myocardial infarction.

As has been pointed out by Parkinson and Bedford,[2] Barnes and Whitten,[7] Whitten,[8] Levine,[9] and Barnes and Ball,[1] myocardial infarction is almost completely confined to the left ventricle. In our series of cases, infarction of the right ventricle was observed only eight times; and in all of these instances there was also involvement of the left ventricle. Whitten[8] and Barnes and Ball[1] have also emphasized that infarction in the left ventricle occurs chiefly in three situations, namely, the anterior and apical, the midventricular, and the posterior basal regions.

When infarction occurs in the anterior and apical section, it involves not only the apex, but frequently also varying portions of the adjacent anterior wall of the left ventricle, adjacent interventricular septum, and occasionally the apical portion of the right ventricle. This type of infarction is caused almost always by occlusion of the anterior descending branch of the left coronary artery or rarely by occlusion of its main trunk. In our series there were ninety-one instances of this type of infarction. In four of these, almost the entire anterior wall of the left ventricle appeared to be involved. In one instance of marked sclerosis of the left coronary artery with occlusion of the circumflex branch, the left ventricle had one infarct at the apex and another at the base. The adjacent interventricular septum was involved in seventeen instances. In seven cases the apical infarct involved the right as well as the left ventricle. In one instance there was also involvement of the base of the anterior papillary muscle.

Infarctions of the middle and lateral portions of the left ventricle are usually caused by occlusion of the circumflex branch of the left coronary artery and occasionally by occlusion of the main trunk of the left coronary vessel. We found ten instances of this type of infarction.

Infarctions of the posterior basal portion of the left ventricle are usually caused by occlusion of the main trunk or a branch of the right

coronary artery and occasionally by occlusion of the circumflex branch of the left coronary artery. The infarct usually involves the basal three-fifths of the posterior wall of the left ventricle, occasionally the adjacent portion of the interventricular septum, and very rarely a portion of the right ventricle. We found sixteen instances of this type of infarction. Concomitant involvement of the septum occurred twice.

In several cases the infarction could not be strictly placed in any of the three types. These were the result of occlusion of the anterior descending branch of the left coronary artery. In two subjects with marked coronary sclerosis and stenosis, but without occlusion of a vessel, the infarct was in the posterior wall of the left ventricle at or near the apex. In one instance of occlusion of the marginal branch of the right coronary artery there was an infarct along the outer border of the right ventricle.

Table IV shows the sites of infarction in our series of cases.

TABLE IV

SITUATION OF INFARCTION

SITE OF INFARCT	ANTERIOR AND APICAL PORTION	MIDVENTRICULAR PORTION	POSTERIOR BASAL PORTION	OTHER SITES
Number	91	10	16	10

Diffuse Fibrosis.—Diffuse fibrosis was noted in ninety-six of the cases and in most instances was confined to the left ventricle. All of the hearts with diffuse fibrosis showed extensive sclerosis and stenosis of the coronary arteries with or without occlusion of one or more vessels. Extensive fibrosis is probably the end-result of chronic diffuse infarction which follows the progressive and gradual narrowing of the coronary arteries. That gradual interference with the coronary circulation leads to diffuse scarring of the myocardium has been stressed by Aschoff,[10] Hunter,[11] Slater,[12] Brown,[13] and others.

Mural Thrombosis.—Mural thrombi were observed in eighty-one, or 54 per cent of the cases, and, as shown in Table V, were found mainly in the left ventricle at the site of infarction. Multiple thrombi were noted in eighteen instances. The auricular thrombi were usually situated

TABLE V

SITUATION OF MURAL THROMBI

CHAMBER INVOLVED	LEFT VENTRICLE	RIGHT AURICLE	RIGHT VENTRICLE	LEFT AURICLE
Number	82	12	7	4

in the appendices and were not directly attributable to the myocardial infarction. This high incidence of mural thrombosis in connection with occlusion of the coronary arteries should be borne in mind by the clinician.

Aneurysm of Heart.—Aneurysm of the heart was found in fifty-seven of the 150 cases, an incidence of 38 per cent. Many observers have commented on the great frequency of aneurysm formation in cases of myocardial infarction. Table VI shows the situation of the cardiac aneurysms. In fifty-six instances the aneurysm was in the left ventricle, most frequently at the apex. In only one case was the right ventricle the seat of an aneurysm.

TABLE VI

SITE OF HEART ANEURYSMS

CHAMBER	APEX LEFT VENTRICLE	ANTERIOR WALL LEFT VENTRICLE	INTERVENTRICULAR SEPTUM	POSTERIOR WALL LEFT VENTRICLE	LATERAL PART LEFT VENTRICLE	APEX RIGHT VENTRICLE
Number	34	10	6	5	1	1

Rupture of Heart.—As has previously been pointed out by Krumbhaar,[14] cardiac rupture is a relatively infrequent sequel of myocardial infarction. In our series, rupture of the heart occurred in only 9 of the 150 cases and was always of the left ventricle. In 7 instances the rupture was through the anterior wall, and in 2 cases, through the posterior wall. There were also two instances of perforation of the interventricular septum, but these were not classified as ruptured hearts. In 6 of the 9 cases the rupture occurred in the stage of acute infarction; in 1 case, through an old healed infarct; and in 2 cases, through the cardiac aneurysm. It is to be borne in mind therefore that, while cardiac rupture usually occurs in the acute stage of softening, it may also occur in a much later stage after the necrotic area has been replaced by fibrous tissue.

Electrocardiograms.—Electrocardiograms were available for study in thirty of the cases. In twenty-three of these, there was found at necropsy an occlusion of one or more of the coronary arteries, while in the remaining seven there was marked coronary sclerosis and stenosis with almost complete occlusion of a vessel. Most of the records were taken shortly before death, many days or even weeks after the probable onset of the occlusion. In a few instances the tracings were made within four days of the acute episode. In one case the electrocardiogram was obtained about seven hours after the onset of the acute symptoms. It was possible to obtain two or more electrocardiographic records in fifteen cases.

In Table VII are presented the more important electrocardiographic details together with the necropsy findings.

With few exceptions the electrocardiograms showed a rapid sinus rhythm, with a range of rate between 90 and 130. Disturbance of the normal rhythm at some stage of the disease was a frequent occurrence. In most instances the interruption was caused by premature contractions, while in a few records there were runs of either paroxysmal tachycardia

or paroxysmal fibrillation. There were also two cases of persistent auricular fibrillation.

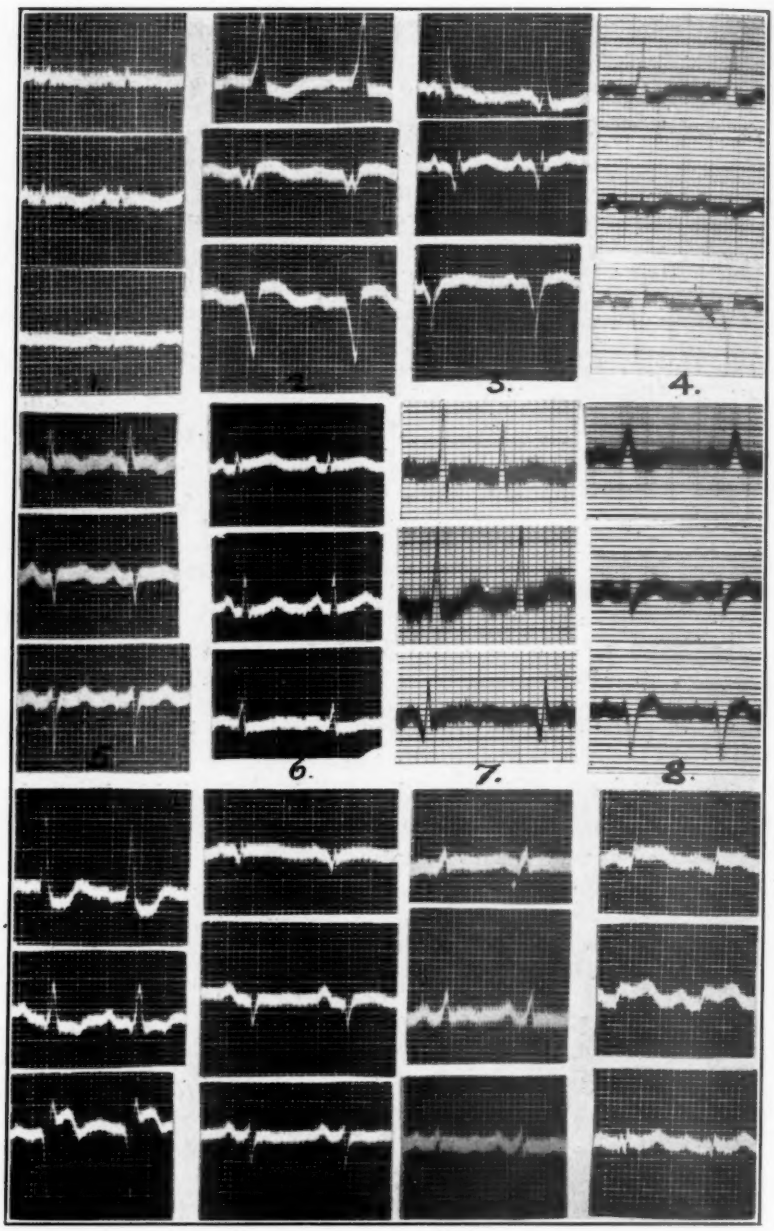

Fig. 1.—Sample tracings of Cases 1 to 12 of this series arranged numerically.

There appeared to be no relationship between coronary artery occlusion and deviation of the electrical axis. The shift was to the left in

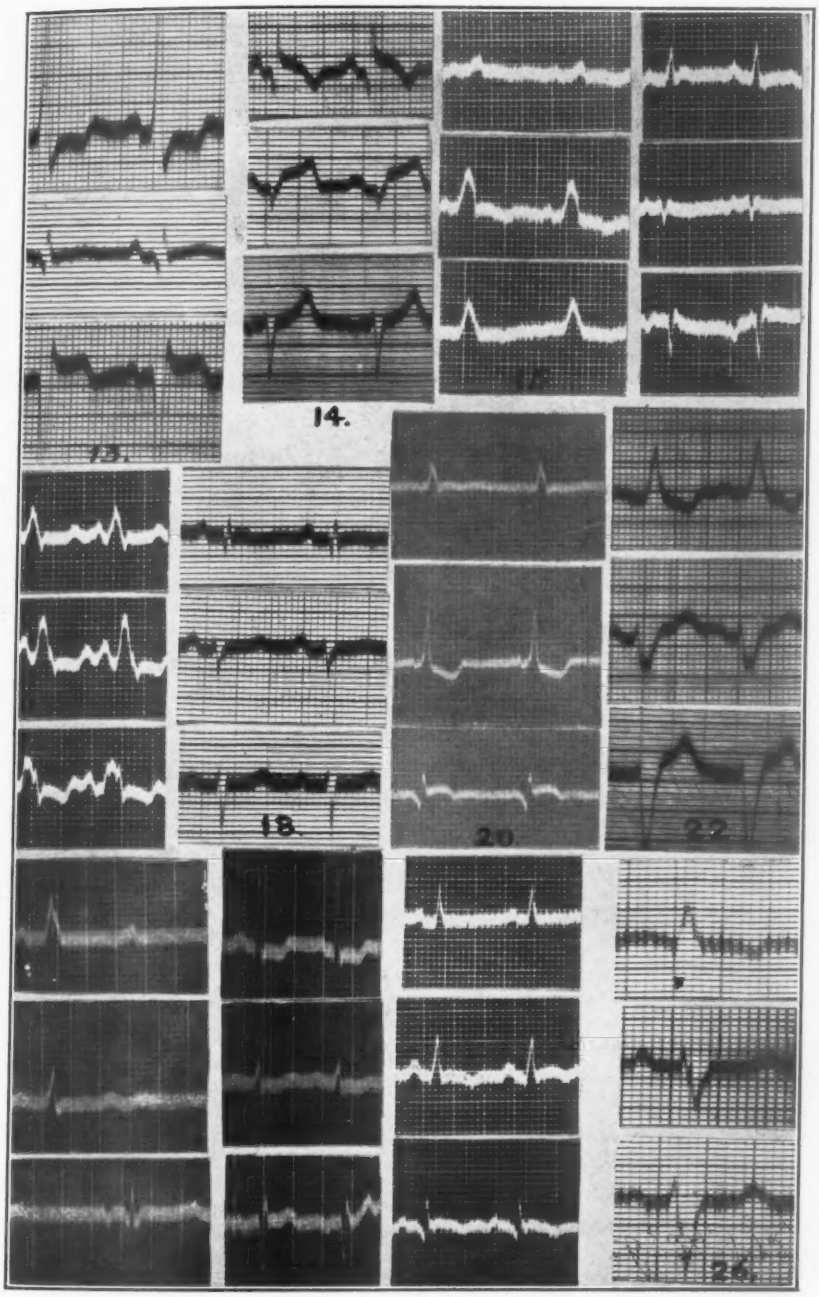

Fig. 2.—Sample tracings of Cases 13 to 26. The record of Case 21 could not be reproduced, and the record of Case 19 is included in Fig. 3.

eight instances of left coronary closure and in two of right coronary closure. No deviation was noted in six cases with anterior apical in-

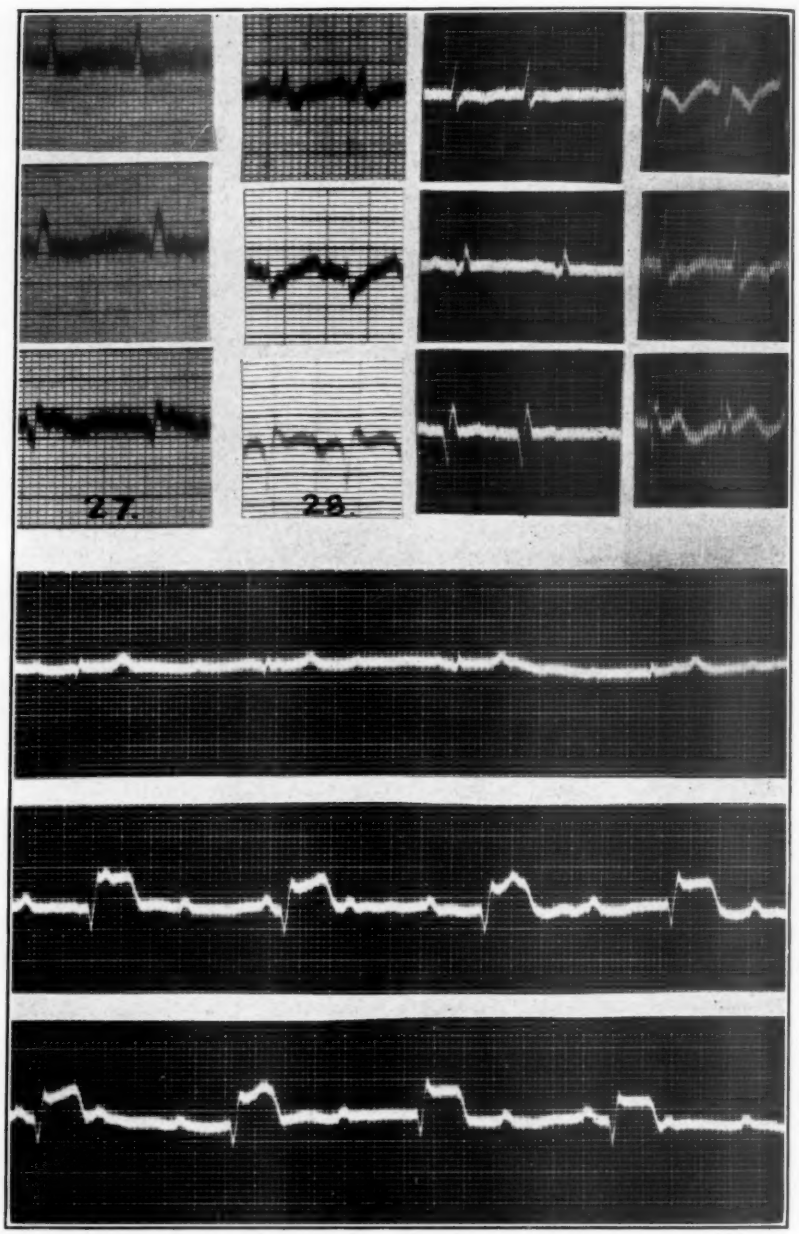

Fig. 3.—Sample tracings of Cases 19 and 27 to 30.

farcts. In two other instances of left coronary closure all the main deflections pointed downward. There were nine records in which a deep Q-wave was responsible for deviation of the axis.

Table VII

Correlation of Necropsy and Electrocardiographic Findings

Case	Site of infarction in left ventricle: Anterior and apical portion	Midventricular portion	Posterior basal portion	Other parts	Diffuse fibrosis	Coronary arteries: Right	Coronary arteries: Left	Pericarditis	Electrocardiograms: Q-waves	Electrocardiograms: Type of T curve
1.	+						Occlusion			
2.	+			Septum	+	Sclerosis	Sclerosis Occlusion			T_2 T_3
3.	+				+	Sclerosis	Sclerosis Occlusion		Q_2	T_3
4.	+					Sclerosis	Sclerosis Occlusion	+	Q_3	T_3
5.	+					Sclerosis	Sclerosis Occlusion	+	Q_1	T_1 T_2
6.	+			Septum		Sclerosis	Sclerosis Occlusion			T_1
7.	+					Sclerosis	Occlusion		Q_2 Q_3	T_3
8.	+					Sclerosis	Sclerosis Occlusion			
9.	+			Septum	+	Sclerosis	Sclerosis Occlusion	+	Q_2 Q_3	T_2 T_3
10.	+					Sclerosis	Sclerosis Occlusion	+	Q_1	T_1
11.	+				+	Sclerosis	Sclerosis Occlusion			
12.	+					Sclerosis	Sclerosis Occlusion	+	Q_1	T_1 T_2
13.	+				+	Sclerosis	Occlusion	+	Q_3	T_3
14.	+			Septum	+	Sclerosis	Sclerosis Occlusion	+	Q_1	T_1 T_2
15.	+					Sclerosis	Sclerosis			T_1 T_2
16.	+					Sclerosis	Sclerosis			
17.	+				+	Sclerosis	Sclerosis			
18.	+					Sclerosis	Sclerosis			
19.	+		+	Septum		Sclerosis Occlusion	Sclerosis Occlusion		Q_2 Q_3	T_2 T_3
20.			+	Septum	+	Sclerosis	Sclerosis Occlusion		Q_3	T_2 T_3
21.			+		+	Sclerosis	Sclerosis almost occlusion	+	Q_3	T_3
22.		+				Sclerosis	Occlusion			T_2 T_3
23.		+				Sclerosis	Occlusion			
24.		+		Septum		Sclerosis	Sclerosis Occlusion	+	Q_3	T_3
25.		+				Occlusion	Sclerosis almost occlusion	+	Q_3	T_2 T_3
26.		+			+	Occlusion			Q_1	T_1
27.					+	Sclerosis	Sclerosis	+	Q_2 Q_3	T_2 T_3
28.	+					Sclerosis	Sclerosis			T_3
29.					+	Sclerosis Occlusion	Sclerosis		Q_3	T_3
30.					+	Sclerosis Occlusion	Sclerosis			T_1 T_2

Interference with impulse conduction was found in fourteen of the patients, in four of whom the delay was noted in both the atrioventricular and bundle-branch systems. Partial atrioventricular block of the first degree, or simple increase of the P-R interval above normal, was present in four patients who at necropsy showed occlusion of the left coronary artery. In two of the cases there was also marked sclerosis and stenosis of the right coronary vessel. In all of the four instances the myocardial infarct was in the anterior apical portion, and in the two cases with the concomitant stenosis of the right coronary artery, there was in addition involvement of the septum.

Complete atrioventricular dissociation was noted in three cases. One of these was probably a digitalis effect and will be omitted from this discussion. In one instance there was marked sclerosis and stenosis of both coronaries with occlusion of the circumflex branch of the left vessel. The infarction was of the midventricular type. There was also a scar with calcification in the upper half of the undefended space above the bundle of His. The other case of complete A-V block was an instance of multiple coronary thrombosis. One thrombus was situated in the main trunk of the right coronary artery proximal to the point where the branch to the bundle of His arises. This was determined by microscopical sections. Another thrombus was found in the anterior descending branch of the left coronary artery, two inches from its origin. The terminal fifth of this vessel was also thrombosed. Fresh infarcts were found in the anterior and posterior walls of the left ventricle and in the interventricular septum. The electrocardiogram in this case was obtained about seven hours after the onset of the acute symptoms.

Eleven patients showed delay in bundle-branch conduction. Four were left bundle-branch blocks (new nomenclature); five were of the arborization type, first described by Oppenheimer and Rothschild;[15] and two showed early defects in the bundle.

At necropsy three of the cases with left bundle-branch block showed occlusion of the anterior descending branch of the left coronary artery, and one case showed occlusion of the circumflex branch of the same vessel. The site of infarction in the former three cases was in the anterior apical portion, and in the latter, in the midventricular portion of the left ventricle.

One of the patients with bundle defect showed an occlusion of the descending branch of the left coronary artery near its origin and almost complete occlusion of the right coronary. Infarcts were noted in the anterior apical portion of the left ventricle and in the interventricular septum near the base. In the second instance of bundle defect there was found an occlusion of the right coronary artery with extensive myocardial fibrosis.

The five cases with arborization block showed marked sclerosis and stenosis of both coronary arteries, with complete occlusion of the right vessel by a thrombus in two instances. Complete occlusion of the left coronary was not observed. A localized infarct was found at the apex of the left ventricle in three cases and in the middle portion of the anterior wall and lateral aspect of the left ventricle in another case. In no instance was infarction of the septum observed. Very extensive myocardial fibrosis was noted in three of the cases.

It is obvious that disturbance in conduction is fairly common in occlusive coronary artery disease. One cannot, however, determine which vessel is involved by the type of block present. It would seem rather that, in those instances showing conduction disturbance, there is extensive and fairly severe involvement of the entire coronary system.

Slurring of the ventricular complex in two or all leads was a constant finding. The M or W type of complex was noted in twelve instances. The QRS amplitude was diminished in sixteen, or 53 per cent of the cases. However, in many instances the voltage remained high.

Pardee,[16] Levine,[9] and others[17, 18] have observed the frequent occurrence of a deep Q-wave in Lead III in cases of coronary artery disease. Its association with occlusion of the right coronary artery has recently been suggested. According to Fenichel and Kugell,[19] a deep Q_3 is indicative of infarction of the septum, particularly its posterior portion.

We found a deep Q_3 wave in 12 of our cases, 6 of which were associated with a Q_2. In 7 of these there was an occlusion of the left coronary artery and in 2, occlusion of the right coronary artery. In one instance both vessels were occluded, and in 2 there was marked stenosis of both coronary vessels. It is to be noted also that marked stenosis of the coronary vessel other than the one occluded was invariably found. The site of infarction was in the anterior apical portion of the left ventricle in 7 instances and in the posterior basal portion in 3 cases. The midventricular type of infarct was recorded twice. Associated septal infarction was noted in 6 instances. Diffuse myocardial fibrosis was almost always present.

The presence of a Q deflection in Lead I was noted in five cases. Four of these showed occlusion of the left coronary vessel with anterior apical infarction. The adjacent septum was involved in one instance. The remaining case showed a closure of the right coronary and a midventricular infarct.

We were particularly impressed with the fact that the eleven patients with pericarditis or pericardial effusion showed the presence of a prominent Q-wave in one or more leads. The significance of this finding will be the subject of further study.

No attempt will be made to draw definite conclusions in regard to the significance of deep Q-waves in coronary artery disease from the study

of this small group of cases. We believe, however, that to regard this change as a localizing sign of myocardial damage is, in the present state of our knowledge, unwarranted.

There has been much discussion in regard to the localization of the myocardial infarct and the artery involved from the pattern of the ventricular complexes in the three leads of the electrocardiogram as described by Parkinson and Bedford,[17] Barnes and Whitten,[7] and Barnes.[20] These workers believe that the T_1 type of tracing indicates infarction of the anterior apical portion and the T_3 type, involvement of the posterior basal portion of the left ventricle. Other investigators, however, are not in accord with this view. Gilchrist and Ritchie[21] in their survey of the literature of proved cases of coronary occlusion conclude that there is no definite localizing electrocardiographic sign of myocardial infarction. Korey and Katz[22] in their experimental work on dogs arrive at a similar conclusion. Wilson and his coworkers,[23] while in agreement with the Parkinson and Bedford rule, have nevertheless noted many exceptions, and suggest that the RS-T segment change may depend upon the localization of the infarct with reference to the endocardial and pericardial surfaces.

In our series there were seven cases of the T_1 type and seventeen of the T_3 type. Six cases remained unclassified. Of these, two showed a shrinkage of the ventricular deflections described by Winternitz.[24]

Five cases of the T_1 group showed a closure of the left coronary vessel with anterior apical infarction. There was additional septal involvement in two instances. There was one case with marked sclerosis and stenosis of both vessels and an anterior apical infarction. The remaining case showed an occlusion of the right coronary artery with a midventricular infarct.

In the T_3 type group there were 10 cases of occlusion of the left coronary vessel with 7 anterior apical, 2 midventricular, and 1 posterior basal infarct. There was associated septal involvement in 3 instances. There was 1 case with occlusion of both coronary arteries with anterior apical, posterior basal, and septal infarctions. There were also 4 instances with marked coronary sclerosis and stenosis, in 2 of which there was an anterior apical, and in 1, a posterior basal infarct. The remaining case showed diffuse fibrosis. The right coronary was found occluded in 2 cases with a midventricular infarct in 1, and diffuse fibrosis in the other instance.

Wilson[23] and later Barnes[25] noted that the changes in the RS-T segment and T deflection in cases of coronary artery occlusion are frequently accompanied by modifications of the initial deflection. These investigators indicate the importance of including the Q deflection in the pattern of the T_1 or T_3 curve. In our series a Q-wave accompanied the T_1 curve in five cases and the T_3 curve in eleven instances.

In many instances the RS-T segment and T-wave changes were in conformity with the rule of Parkinson and Bedford; nevertheless, frequent exceptions were noted. It seems to us, therefore, that one cannot regard the standard three lead electrocardiogram as a definite localizing sign of myocardial infarction.

II. *Syphilitic Group*

In this series of cases the underlying pathological condition was a moderate degree of syphilitic aortitis. There were ten cases in this group. In nine of these, occlusion of one or both coronary orifices was caused by the luetic process in the aorta, and in one, the main trunk of the right coronary vessel from the orifice down to its bifurcation was occluded by a thrombus. The ostium of the right coronary artery was found occluded eight times, and of the left coronary, four times. There were thus two instances with occlusion of both the right and the left coronary vessels.

We were particularly impressed with the relatively good condition of the coronary arteries in these subjects. In only five of the cases was there an appreciable degree of sclerosis, which did not appear, however, to have played any rôle in the causation of the occlusion. In the case with a thrombus in the right coronary artery the vessels were apparently free from sclerosis. Unfortunately, the coronary arteries in this instance were not examined microscopically for signs of syphilitic involvement. It is, therefore, impossible to say whether or not syphilis played a rôle in the production of the thrombus. In this connection, it is important to note that modern pathologists do not regard syphilis as an etiological factor in the production of arteriosclerosis.

A number of other interesting features in this group deserves consideration. The heart weight as determined in five cases ranged from 250 to 970 gm. No conclusion as to the size of the heart could be drawn from so small a series. Myocardial infarction was observed in one case and was situated in the apical portion of the right ventricle near the septum. In one instance there was extensive fatty degeneration of the myocardium. Pericarditis was found in four of the cases; it was subacute fibrinous in one case; and in three instances it was chronic adhesive in character with superimposed calcification in one of them. It was difficult to say whether or not the old fibrous pericarditis was in any way related to the occlusion of the coronary orifices. A slight degree of diffuse fibrosis of the myocardium was observed in three cases. Mural thrombi were found in two cases; in one, the thrombus was situated at the apex of the right ventricle; and in the other, there were thrombi in both auricles. The subjects ranged in age from thirty to seventy-five years. There was a decided predominance of males, as there were only two women in this group.

Electrocardiographic records were made of three patients in this group. Inversion of T_1 with a depressed S-T_1 segment and upright T_3 were present in all three instances, in two of which the R-T_3 segment was elevated. Bundle-branch block associated with partial atrioventricular block was noted in two instances. Pulsus alternans was present in one case. Auricular fibrillation as a terminal event was observed in one instance. A deep Q_3 was noted once in combination with bundle-branch block.

We are presenting the findings in this small group of cases without attempting to draw definite conclusions. It seems to us that this subject merits further study.

III. *Miscellaneous Group*

In this series of cases a variety of causes other than arteriosclerosis or syphilis were responsible for the coronary occlusion. There were 4 instances of vegetative endocarditis with embolization of the coronary vessels. There was 1 case of rheumatic pancarditis with coronary thrombosis. In 1 instance the coronary vessel was occluded by neoplastic metastasis. There were also 2 remarkable cases of periarteritis nodosa with extensive occlusion of the coronary arteries.

In the 4 cases of bacterial endocarditis, vegetations were found superimposed on old rheumatic valve lesions in 3 instances, and on a congenital bicuspid aorta in 1 instance. The embolism caused a coronary thrombosis in 3 cases and a mycotic aneurysm in 1. The left coronary artery was found involved in 3 instances and the right coronary vessel in 1. The mycotic aneurysm, the size of a walnut, was situated in the left coronary artery. As pointed out by Packard and Wechsler,[26] Cox and Christie,[27] and Pretty,[28] this type of coronary aneurysm is exceedingly rare. Recent myocardial infarcts were observed in 3 of the cases and were situated in the anterior wall of the left ventricle in 2 instances, and in the posterior wall of the same chamber in 1 instance. Fibrinous pericarditis, which is a rare finding in subacute bacterial endocarditis, was observed in the subject with the coronary aneurysm. Evidence of embolic phenomena in other viscera was found in every case.

Electrocardiograms were available in three of the cases. Two of these showed the presence of paroxysmal auricular fibrillation, which is a comparatively rare finding in bacterial endocarditis. It is not unlikely, therefore, that the coronary occlusion was responsible for the development of the arrhythmia. The tracings showed no other remarkable changes.

The closure of a coronary artery by a neoplasm is a very unusual occurrence. In our case the subject had an epithelioma of the tongue with very extensive metastasis to the cervical lymph nodes, lungs and pleurae,

heart, liver, kidneys, right adrenal, peritoneum, and vertebrae. In the heart the tumor tissue was found in the posterior wall of the left ventricle and in the right coronary artery.

Involvement of the coronary arteries in rheumatic fever has been observed by a number of workers, notably Aschoff,[29] Giepel,[30] Coombs,[31] Swift,[32] Pappenheimer and von Glahn,[33] Slater,[12] and Perry.[34] Endarteritis with swelling and proliferation of the endothelium is not infrequently encountered. This may cause not only a constriction but at times also a complete occlusion of the artery. Rarely complete or partial closure of the lumen may be caused by a thrombus that has formed in the injured vessel. Not infrequently a coronary artery may be involved in a process of submiliary nodule formation which may cause marked compression of the lumen and subsequent closure of the vessel.

In our series there was one case of rheumatic pancarditis with thrombotic occlusion of both coronary arteries; an endarteritic process was observed in many of the blood vessels, including the coronaries. In each coronary artery the thrombus was found in the main stem near the orifice. There were also thrombi in the right main branch of the pulmonary artery, in the right popliteal artery, and in the inferior vena cava. That the intima of the large vessels is not infrequently involved in rheumatic fever has been stressed by Jores,[35] Stumpf,[36] and more recently by Pappenheimer and von Glahn.[33] Thrombosis in the veins as well as arteries has been observed also by Libman[37] and Hess.[38]

Since its first comprehensive description by Kussmaul and Maier[39] in 1866, periarteritis nodosa has been a subject of great interest to many investigators. A great deal of attention has been focused particularly on the detailed pathological changes in the blood vessels. The earliest change observed in this remarkable inflammatory disease of the arteries is necrosis of the media with destruction of the elastic tissue. This is followed by an infiltration of the vascular wall with a cellular exudate. In this acute stage the predominating cells are polymorphonuclear neutrophiles, although a few lymphocytes, eosinophiles, and plasma cells may also be present. The inflammatory reaction may then extend to the perivascular zone. When the acute process begins to subside, granulation tissue wanders in from the adventitia and pervades the entire vascular wall and even perivascular area. During the process of repair the polymorphonuclear leucocytes are replaced by eosinophiles, lymphocytes, and plasma cells.

During the inflammatory and reparative phases of the disease certain other remarkable changes may occur in the involved blood vessels. There may be a proliferation of the subendothelial connective tissue with consequent encroachment on the lumen of the vessel. The intimal lesion may also lead to the formation of secondary thrombi. In other arteries the wall is weakened, and small aneurysms are formed along the course

of the vessel. These aneurysms frequently rupture. Thrombus formation in the aneurysms is common. Occasionally in the process of healing there is replacement of the injured vascular wall by scar tissue which may form in and around the artery. The usual result of the various arterial changes is to obstruct the vessel and hinder the supply of blood to the involved viscera.

In our study we found two cases of periarteritis nodosa with involvement of the coronary arteries. Both subjects were males, and their ages were fifteen and twenty-one years, respectively. In each instance both the right and left coronary arteries were extensively involved, with occlusion of the vessels in numerous places. The coronary arteries showed nodular thickenings along their course and had numerous thrombi. In some of the vessels there was marked narrowing of the lumen by the fibrous tissue replacement in the vascular wall. In one of the cases the coronary arteries showed numerous aneurysms, many of which contained thrombi. In this instance death was caused by rupture of one of these aneurysms into the pericardial cavity. This case was reported in detail by Vance and Graham.[40] Fibrinous pericarditis was present in one of the cases. Multiple infarcts of the liver, spleen, and kidneys were observed in both instances. The hearts weighed 340 and 430 gm., respectively. One of the subjects showed also a terminal vegetative endocarditis with a mural thrombus in the left auricle. A rather interesting, and perhaps significant, finding in both cases was the presence of tuberculous bronchial and mesenteric lymph nodes. In the case reported by Vance and Graham, changes typical of periarteritis nodosa were observed also in the arteries of the liver, kidneys, spleen, pancreas, mediastinum, epididymis and gastrointestinal tract.

SUMMARY

1. We have analyzed a series of 168 cases of occlusive diseases of the coronary arteries, dividing them into the atherosclerotic, syphilitic, and miscellaneous groups.

2. The pathological features in the atherosclerotic group were presented in detail. Particular notation was made of the sites of myocardial infarction and of the coronary vessels occluded. Attention was drawn to the predominant involvement of the left coronary artery with the resulting anterior apical type of infarction. The frequency of mural thrombosis and of cardiac aneurysms was stressed.

3. The electrocardiographic records in thirty of the cases were correlated with the necropsy findings. The tracings invariably showed evidence of myocardial damage. While in many instances the QRS-T segment and T-wave changes were in conformity with the rules of Wilson and of Parkinson and Bedford, there were also frequent exceptions. It

was our impression, therefore, that one cannot regard the three-lead electrocardiogram as a definite localizing sign of myocardial infarction.

4. An analysis was presented of a group of ten cases of syphilitic aortitis with closure of the coronary orifices. In nine of these, occlusion of one or both coronary ostia was caused by the syphilitic process in the aorta, and in one, the main trunk of the right coronary vessel was occluded by a thrombus. Electrocardiograms were available in three of the cases. These showed various abnormal findings. No attempt was made to draw conclusions from so small a series.

5. A miscellaneous group of eight cases with coronary artery occlusion was presented. Four of these were instances of vegetative endocarditis with embolization of the coronary vessels, producing a thrombosis in three of the cases, and a mycotic aneurysm in one. The electrocardiograms showed the presence of paroxysmal auricular fibrillation in two instances. In this group were also included a case of neoplastic invasion of a coronary artery, a case of rheumatic disease of the vessels, and two remarkable instances of periarteritis nodosa with very extensive involvement of the coronary system. We reviewed the detailed pathological changes in the blood vessels in the rheumatic and in the periarteritis nodosa cases.

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THE DELAY IN THE ONSET OF EJECTION OF THE LEFT VENTRICLE IN BUNDLE-BRANCH BLOCK*†

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RECENTLY, the location of the lesion in so-called bundle-branch block has become the subject of considerable controversy. The opinions expressed can be placed in three categories:

(1) The classical interpretation asserts that the common bundle-branch type of intraventricular block (QRS_1 upright, QRS_3 inverted) indicates a lesion of the right bundle branch, and the uncommon type, (QRS_1 inverted, QRS_3 upright) a lesion of the left branch.

(2) The modern interpretation, arrived at on theoretical grounds by Fahr[1] and promulgated by Wilson and his school,[2] asserts the exact opposite of the classical view.

(3) The interpretation first advanced by one of us (Katz[3]), and supported by experimental evidence,[4] maintains that the direction of the QRS complex in the electrocardiogram of intraventricular block does not necessarily determine the location of the involved bundle branch, since other factors, such as the position of the heart, the relative hypertrophy or dilatation of the chambers, etc., influence the contour of the electrocardiogram.

When the evidence pertaining to the subject is examined, one finds a number of contradictions. Thus, autopsy examination shows that in some instances the right (Taussig,[5] Hill[6]), in others the left bundle branch (Oppenheimer and Pardee[7]) is involved when the electrocardiogram shows the common bundle-branch type of intraventricular block. The more recent work of Mahain[8] has shown that a careful inspection of serial sections will reveal lesions in both bundle branches in most, if not all, hearts with such electrocardiograms; an opinion with which Yater[9] is in accord.

The original electrocardiographic interpretation of bundle-branch type of block was based on the electrocardiograms obtained in dogs by Lewis.[10] Wilson and his coworkers[2] recently arrived at the conclusion that the electrocardiograms of left and right bundle-branch block had been reversed in the classical terminology. Their deduction was based on the time of appearance of initial negativity in the two ventricles in so-called bundle-branch block, as given presumably by "semidirect" leads from the chest wall over the right and left ven-

*From the Heart Station, Michael Reese Hospital, Chicago.
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tricles. The criterion used by them to indicate activation beneath the electrode has not been conclusively shown to be adequate for this purpose. It is interesting to point out that further experience by Wilson and others[11] with this procedure has shown several exceptions to their own terminology and forced these workers to concur in the opinion expressed in our laboratory[4] that other things besides the block can determine the direction of the QRS complex in so-called bundle-branch block.

A second line of evidence for Wilson's interpretation is based on the appearance of artificially induced ventricular extrasystoles in patients with pericardial fistulas, where it was found by several investigators[12] that the direction of the QRS complex of extrasystoles from the two ventricles was just the reverse of that anticipated on the classical interpretation. This evidence would be more convincing if the hearts used had been normal in size, shape, and position.

A third line of approach to this problem was attempted recently. Nichol[13] argued that in left bundle-branch block one might expect a lag in the onset of systole and ejection in the left ventricle. This could be easily observed by measuring the time interval between the beginning of the QRS complex which marks the onset of stimulation of the ventricles and the start of the rise of the optically recorded subclavian pulse which marks the onset of ejection of blood from the left ventricle. The duration of this interval (designated the Q-E interval) in a group of normal patients was compared with that in a group with intraventricular block of the common bundle-branch type. He found that the average Q-E interval was prolonged in the common bundle-branch block type, indicating to him that the block was in the left bundle branch. A similar observation and deduction was also made independently by Wolferth and his collaborators.[14*] The assumption made in both of these investigations that all electrocardiograms with common bundle-branch type of block are due to involvement of the same bundle branch cannot be conceded. It is not sufficient therefore to compare the average duration of the Q-E interval but actually to determine whether or not the Q-E interval falls outside the control range in each instance. An examination of the data published by these workers shows several instances in which the Q-E interval was

*The other measurements of Wolferth and his associates are subject to severe criticism. It is difficult to understand why the Q-C interval where C is the beginning of the rise of the C-wave in the venous pulse, should not be prolonged as much as the Q-E interval in their patients with bundle-branch block, since the rise of the C-wave, we have found, is coincident with the rise of the arterial pulse wave (cf. also Wiggers[15]). The asynchronism of −0.04 to +0.07 second found by them to exist between the start of ejection of the right and left ventricles in patients with prolonged QRS complexes as shown by x-ray-time curves of the aorta and pulmonary artery was of the same order of magnitude as in patients with split first sounds without such QRS prolongation (viz., −0.06 to +0.06 second). Their observation that in instances where common bundle-branch type of intraventricular block is associated with a split second sound, the second element is a left-sided event as judged by comparison with the arterial and venous pulses, ignores the fact that many instances of this type of block are found without such splitting of the second sound. The significance of these measurements of Wolferth and his coworkers must, therefore, be held *sub judice* for the present.

within the range found in their controls. We therefore deemed it advisable to determine the Q-E interval in a further larger series of

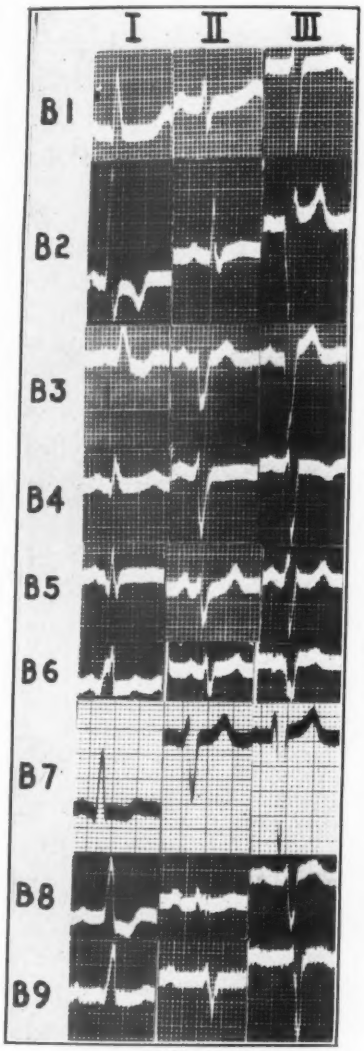

Fig. 1.

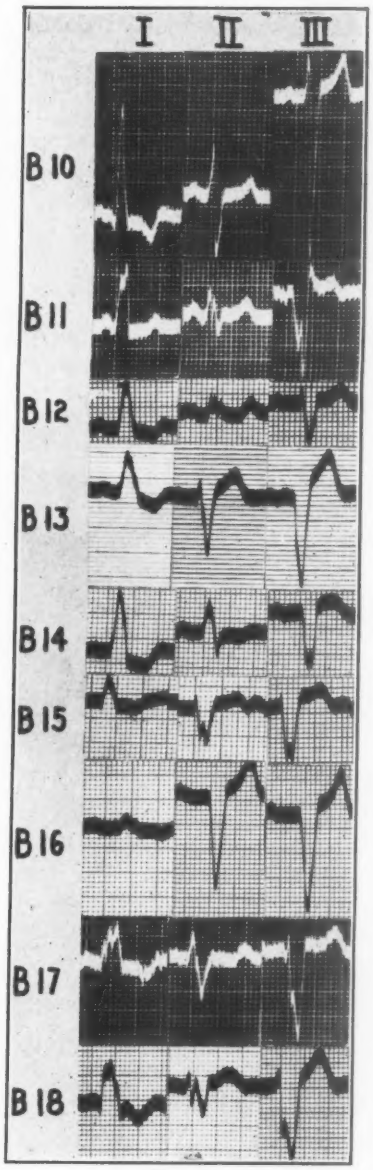

Fig. 2.

Fig. 1.—The appearance of the electrocardiogram in Cases B1 to B9 referred to in Table III.

Fig. 2.—The appearance of the electrocardiogram in Cases B10 to B18 referred to in Table III.

subjects having electrocardiograms of so-called bundle-branch block and in a further series of controls.

The present report is based on observations made on 9 normal individuals, 30 patients with heart disease having a QRS duration of 0.10 second or less and 29 patients having intraventricular block as shown by the presence of a QRS duration of 0.12 second or more. These latter included 18 patients with common bundle-branch type of block

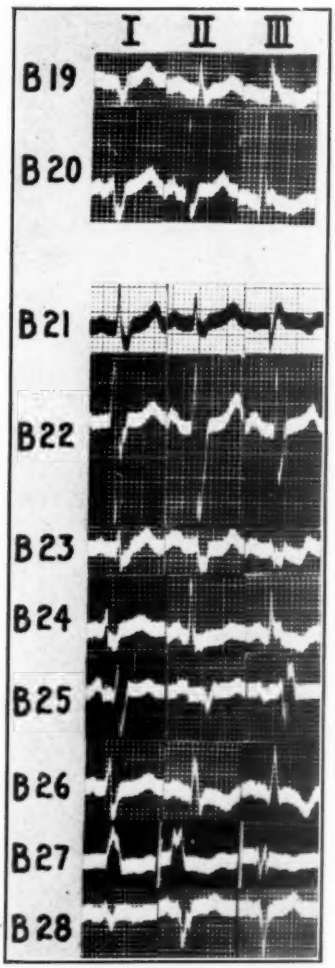

Fig. 3.—The appearance of the electrocardiogram in Cases B19 to B28 referred to in Table III.

(the QRS duration in 9 being 0.12 – 0.13 second and in the other 9, 0.14 – 0.20 second), 3 patients with the uncommon bundle-branch type of block (the QRS duration being 0.12 – 0.20 second), and 8 patients with nondescript indeterminate types of intraventricular block, including the arborization type (the QRS duration being 0.12 – 0.15 second). The appearance of the standard three leads of each

of the patients with intraventricular block at the time the Q-E interval was determined is shown in Figs. 1, 2, 3, and 4.

The Q-E interval was obtained by measurement from photographs of the right subclavian pulse obtained with the Frank capsule and the Katz-Baker double slit lamp, registered simultaneously with Lead II of the electrocardiogram. The absence of parallax was checked in every instance by recording the position of points with the camera stationary.

DISCUSSION

The results of this analysis are assembled in Tables I to III. The measurements given are carried to the second decimal place since experience has shown that the measurements are accurate only to ± 0.01 second. Each measurement represents the mean of 3 to 4 beats.

The range of Q-E duration found in our normal series is comparable with that reported by Nichol in 19 normals and by Wolferth and his coworkers in 9 normals (cf. Table I); taking all 37 instances the range found in normals is from 0.10 to 0.17 second. Similarly the range for our abnormal controls was equivalent to that reported by Nichol in 23

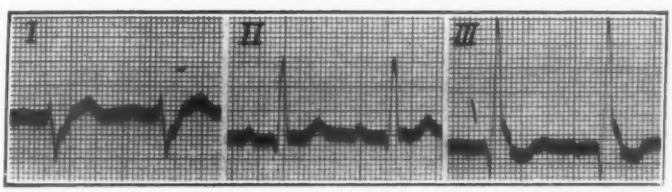

Fig. 4.—The appearance of the electrocardiogram in Case B20A referred to in Table III.

cases and by Wolferth and his coworkers in 7 cases (cf. Table II); the range found in these 60 cases is from 0.08 to 0.19 second, or, excluding the instance of 0.19 second found in a patient with auricular fibrillation, the range is from 0.08 to 0.16 second.

Inspection of Table III shows that the Q-E intervals were within the control range in the three instances with the uncommon bundle-branch type and in all instances with the nondescript indeterminate types of intraventricular block. The Q-E interval was well within the control range in all but one instance with the common bundle-branch type of intraventricular block having a QRS duration of 0.12 to 0.13 second. The one exception (B7) had a Q-E interval of 0.19 second, which is beyond the range found in the controls. In the group of common bundle-branch type of intraventricular block and QRS duration 0.14 second or longer, one instance (B10) had a Q-E interval at the lower range of the controls; three had Q-E intervals just beyond the range found in the controls; only two instances were found with Q-E intervals definitely outside the control range, one being an instance with auricular fibrillation. A similar inspection of the cases

TABLE I

DURATION OF Q-E INTERVAL IN NORMAL SUBJECTS

SUBJECT	QRS SEC.	Q-E SEC.
N1	0.08	0.10
N2	0.08	0.10
N3	0.08	0.10
N4	0.08	0.11
N5	0.07	0.12
N6	0.08	0.12
N7	0.06	0.13
N8	0.09	0.14
N9	0.08	0.16

Range of Q-E interval.
Our results 0.10 – 016 sec.
Nichol's results 0.11 – 0.17 sec.
Results of Wolferth et al. 0.10 – 0.15 sec.

TABLE II

DURATION OF Q-E INTERVAL IN CARDIAC PATIENTS WITH QRS DURATION 0.10 SECOND OR LESS

SUBJECT	QRS SEC.	Q-E SEC.
C1	0.08	0.08
C2	0.06	0.10
C3	0.10	0.10
C4	0.07	0.12
C5	0.08	0.12
C6	0.08	0.12
C7	0.08	0.12
C8	0.08	0.12
C9	0.08	0.12
C10	0.08	0.12
C11	0.10	0.12
C12	0.10	0.12
C13	0.10	0.12
C14	0.08	0.12
C15	0.10	0.13
C16	0.05	0.13
C17	0.10	0.13
C18	0.08	0.14
C19	0.07	0.14
C20	0.08	0.14
C21	0.07	0.14
C22	0.10	0.14
C23	0.08	0.14
C24	0.08	0.15
C25	0.08	0.16
C26	0.08	0.16
C27*	0.06	0.16
C28*	0.06	0.16
C29*	0.07	0.16
C30*	0.05	0.19

Range of Q-E interval, our results 0.08 – 0.19 sec.
Nichol's results 0.08 – 0.15 sec.
Results of Wolferth et al. 0.08 – 0.13 sec.
Range of Q-E interval excluding cases with auricular fibrillation 0.08 – 0.16 sec.
*Auricular fibrillation.

reported by Nichol shows that the Q-E interval of at least two of his cases fall within the upper limit of the control range and only in two of his cases is the Q-E interval definitely prolonged. Six of the cases cited by Wolferth and his coworkers have Q-E intervals within the upper limit of the control range and only one case, and that one having auricular fibrillation, had a definitely prolonged Q-E interval.

TABLE III

DURATION OF Q-E INTERVAL IN INTRAVENTRICULAR BLOCK

SUBJECT	QRS SEC.	Q-E SEC.	
A. COMMON BUNDLE-BRANCH BLOCK TYPE, QRS DURATION 0.12 – 0.14 SECOND			
B1	0.12	0.12	Range of Q-E interval, our results 0.12 – 0.19‡¶
B2	0.12	0.12	
B3	0.12	0.12	
B4	0.12	0.14	
B5	0.12	0.14	
B6	0.12	0.14	
B7	0.12	0.19	
B8	0.13	0.13	
B9	0.13	0.14	
B. COMMON BUNDLE-BRANCH BLOCK TYPE, QRS DURATION 0.14 SECOND OR MORE			
B10	0.14	0.10	‡ Nichol's results 0.15 – 0.20 sec.¶
B11	0.14	0.17	‡ Results of Wolferth, et al. 0.15 – 0.18 sec. (0.25*)¶
B12	0.14	0.21	
B13	0.16	0.16	Range of Q-E interval, our results 0.10 – 0.23 sec.‡¶
B14	0.16	0.17	
B15	0.16	0.18†	
B16	0.16	0.18‡	
B17	0.18	0.18	
B18*	0.20	0.23	
C. UNCOMMON BUNDLE-BRANCH BLOCK TYPE, QRS DURATION 0.12 SECOND OR LONGER			
B19	0.12	0.09	Range of Q-E 0.09 – 0.14 sec.
B20	0.14	0.14	
B20A	0.20	0.08	
D. INDETERMINATE BLOCK INCLUDING ARBORIZATION TYPES, QRS DURATION 0.12 SECOND OR LONGER			
B21	0.12	0.09§	Range of Q-E interval 0.09 – 0.16 sec.
B22	0.12	0.10	
B23	0.12	0.10	
B24	0.12	0.13	
B25	0.12	0.14	
B26	0.14	0.14	
B27	0.14	0.16	
B28	0.15	0.15	

*Auricular fibrillation.

†Ventricular extrasystole, with QRS same direction as that of block, had duration of QRS of 0.16 and Q-E of 0.21 sec.

‡Ventricular extrasystole, with QRS opposite to that of block, had QRS duration of 0.12 and Q-E of 0.19 sec.

§Ventricular extrasystole, with QRS opposite in direction to that of block, had QRS duration of 0.15 and Q-E of 0.15 sec.

¶Nichol and Wolferth et alia did not separate common types of bundle-branch block into these two groups.

The interpretation of the significance of the Q-E interval is not so simple as it might seem at first sight. In reality the Q-E interval is the summation of a number of variables.

(1) A latent period exists between the onset of stimulation of the ventricles and the time when the electrical stresses so set up produce enough of a resulting potential to deflect the string of the electrocardiograph at ordinary sensitivity. This, as Nichol's[13] measurements have shown, may vary between leads as much as ± 0.04 of a second.

(2) A latent period exists between the onset of the QRS complex and the onset of mechanical systole as shown by the intraventricular pressure curves in the dog, which varies from 0.01 to 0.13 second (Wiggers[16]). This latency is not the same for both ventricles, there being a definite asynchronism in the dog of about ± 0.01 to ± 0.03 second (Katz[17]), a value in accord with the asynchrony of ejection of ± 0.02 second found by Wolferth and his coworkers[14] in man on analyzing the x-ray-time curves of the aorta and pulmonary artery.

(3) A period of isometric contraction exists, during which the left ventricle is getting up steam, as it were, before it begins to eject blood. This varies in duration in man from 0.025 to 0.09 second (Katz and Feil[18]).

(4) A time lag exists transmitting the pulse from the aorta where it is started to the point of registration. This is not fixed, because the distance the pulse has to travel and its rate of travel both are variable. Rough calculations would suggest the variation on this account to be about 0.02 to 0.04 second.

(5) The time of stimulation of the left ventricle relative to the rest of the heart is the factor which depends on the location of the block.

It is the variable summation of these time factors and the slight error of possibly ± 0.01 in determining the two points for measuring the Q-E interval which account for the relatively wide range of Q-E duration in the control series. Because of this variability, we feel that the interpretation of probable left ventricular lag and therefore of "functional" left bundle-branch block should only be made in instances where the Q-E interval is 0.18 of a second or longer. Similarly the probable absence of left ventricular lag and therefore of "functional" left bundle-branch block should be made only in instances where the Q-E interval is 0.14 second or less. The range between 0.14 and 0.18 second in our opinion is without value in determining the presence or absence of "functional" left bundle-branch block. Perhaps it would be more accurate and preferable to speak of delayed conduction to large regions of the right or left ventricle instead of "functional" right or left bundle-branch block. However, the latter terminology will be used here for the sake of brevity.

On this basis probably only one instance of "functional" left bundle-branch block was present in Group A of Table III. The rest, though being of the common bundle-branch type of intraventricular block, are probably not "functional" left bundle-branch block and therefore

presumably "functional" right bundle-branch block. In Group B of Table III, more advanced degrees of the common bundle-branch type of intraventricular block: one case is probably not a "functional" left bundle-branch block but a "functional" right bundle-branch block; five are probably "functional" left bundle-branch blocks, no opinion being possible in the remaining three. All three instances of uncommon bundle-branch block type are probably not "functional" left bundle-branch block but "functional" right bundle-branch block. A similar interpretation can be made in all but two of the patients with nondescript indeterminate types of intraventricular block; in these two exceptions no opinion can be passed. Case B20A is particularly interesting because the uncommon bundle-branch block type was of relatively recent occurrence and had replaced a long standing common bundle-branch block type. We must, therefore, conclude that in this patient either the new bundle-branch block had completely replaced the old or the old bundle-branch block was located in the same bundle as the new.

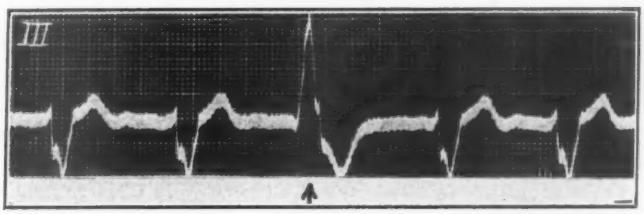

Fig. 5.—Lead III of electrocardiogram obtained in Case B18, showing the interruption of the predominant beats by an occasional beat (↑) of the opposite type.

The evidence obtainable from this study points to the conclusion that the direction of the QRS complex in the standard three leads cannot be used to locate functionally significant bundle-branch block. This study emphasizes again that other factors besides block determine the direction of the QRS complex. In view of these facts it would be wise, it seems to us, to avoid attempting to locate the block. We would advocate instead the use of the terms common bundle-branch type, uncommon bundle-branch type, indeterminate type and perhaps arborization type of intraventricular block in describing such electrocardiograms unless one can ascertain from other determinations, such as the Q-E interval, where the block is located.

The Q-E intervals of the ventricular extrasystoles encountered in our records were longer in each of three subjects than those of the predominant beats in the series, regardless of whether the direction of the QRS complex was the same or opposite to that of the predominant beats. This is at least partly to be explained as an effect of the prematurity of these beats. For example, this effect of cycle length on the Q-E interval was noted on another occasion in Case B18, a pa-

TABLE IV

CASE B18 (LEAD III)

BEAT	QRS SEC.	Q-E SEC.	CYCLE LENGTH* SEC.	TYPE OF COMPLEX	
9	0.20	0.26	0.78	C†	Strip #1
3	0.22	0.25	0.82	C	
1	0.22	0.24	0.84	C	
5	0.22	0.25	0.86	C	
6	0.22	0.26	0.90	C	
7	0.22	0.24	0.90	C	
2	0.23	0.23	1.16	C	
8	0.22	0.23	1.18	C	
4	0.22	0.21	1.24	C	
1	0.15	0.21	0.96	U† (small)	Strip #2
3	0.22	0.27	0.94	C	
1	0.21	0.25	0.93	C	Strip #3
2	0.23	0.19	0.90	U (large)	
1	0.22	0.22	1.10	C	Strip #4
2	0.22	0.20	1.04	U (large)	
3	0.22	0.23	1.00	C	
1	0.14	0.18	1.00	F†	Strip #5
2	0.20	0.25	1.04	C	

*Cycle length is the duration of the cycle starting with the onset of QRS of the beat preceding the one measured.

†C complex is of the common bundle-branch type of intraventricular block.
U complex is of the uncommon bundle-branch type of intraventricular block.
F complex here was polyphasic and small in Lead III.

tient with "functional" left bundle-branch block and auricular fibrillation, where a strip of nine consecutive beats was measured. It was found that the Q-E interval tended to lengthen as the interval between beats shortened (Table IV, strip No. 1).

This case (B18) at one time presented a very interesting condition; namely, on one occasion it was found that over a period of minutes several abnormal ventricular complexes appeared interspersed among the predominant beats. Some of these were of the type exactly opposite to the predominant beats, resembling the uncommon bundle-branch type of block. Because these beats did not occur prematurely (cf. Fig. 5), we interpreted them as being not ventricular premature systoles but in all likelihood beats of supraventricular origin conducted through the ventricles differently from the other beats.

The Q-E interval of three such beats was measured and compared with predominate beats immediately preceding or following them, having about the same period of preceding diastole (cf. Table IV). In each instance the Q-E interval was in the range considered by us to indicate "functional" left bundle-branch block. Two of these beats had a definitely shorter Q-E interval than the comparable predominate beats, but in the third the duration was very little different. One beat (F strip #5 of Table IV) was a fusion form; it also had a Q-E

interval duration just beyond the normal range, making it probable that there was a "functional" left bundle-branch block here also.

The implication of this case seems clear, namely that beats with uncommon bundle-branch type of intraventricular block may accompany "functional" left bundle-branch block. This does not preclude the presence of "functional" right bundle-branch block; since, even if both branches were involved, the Q-E interval would show only the involvement of the left. It follows from this that the presence of a "functional" left bundle-branch block shown by the Q-E interval in any case does not rule out the possibility of a "functional" right bundle-branch block also being present. However, a prolonged QRS complex without a prolonged Q-E suggests the presence of "functional" right bundle-branch block only.

SUMMARY

The Q-E interval, from the beginning of the QRS complex to the onset of ejection of the left ventricle as given by the rise of the subclavian arterial pulse, was determined in 9 normal subjects, in a control group of 30 patients with heart disease without intraventricular block (QRS duration 0.10 second or less), and in 29 patients with intraventricular block of various sorts as shown by a QRS duration of 0.12 second or longer. In the control groups the Q-E interval varied from 0.08 to 0.16 second (to 0.19 second when cases with auricular fibrillation are included).

This wide range in Q-E duration is due to the fact that the Q-E interval measures a number of variable factors besides the relative time of stimulation of the left ventricle.

In evaluating the meaning of the Q-E interval in individual instances of intraventricular block, it is inferred from the above that the range between 0.14 and 0.18 second is of no value in determining the presence or absence of "functional" left bundle-branch block. In intraventricular block a Q-E interval less than 0.14 second indicates the probable absence of "functional" left bundle-branch block and therefore suggests "functional" right bundle-branch block. In intraventricular block a Q-E interval longer than 0.18 second suggests the probable presence of "functional" left bundle-branch block but does not exclude the simultaneous presence of "functional" right bundle-branch block.

On this basis it was shown that the common bundle-branch type of intraventricular block included instances of "functional" right as well as "functional" left bundle-branch block.

It is therefore concluded that these results confirm our previous view that the direction of the QRS complex is determined by other factors besides the block, and it cannot be used to locate the bundle branch involved in intraventricular block. Some other indication such

as the Q-E duration must be employed if the location of block is desired. It is preferable, we believe, to describe intraventricular block, for the present at least, as (1) common bundle-branch type, (2) uncommon bundle-branch type, or (3) indeterminate types.

We are grateful to Drs. W. W. Hamburger, Sidney Strauss, J. Plaut, and W. Priest for sending to us some of the patients used in this study.

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A NEW AND SIMPLE METHOD OF AVOIDING HIGH RESISTANCE AND OVERSHOOTING IN TAKING STANDARDIZED ELECTROCARDIOGRAMS

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FOLLOWING the introduction of the string galvanometer, Einthoven suggested a standardization for electrocardiograms such that a one centimeter excursion in the final record would represent a change of one millivolt potential difference. This degree of sensitivity to test currents is readily obtainable in all string galvanometers.

Fig. 1.

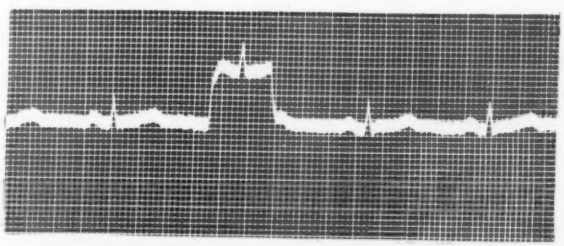


Fig. 2.

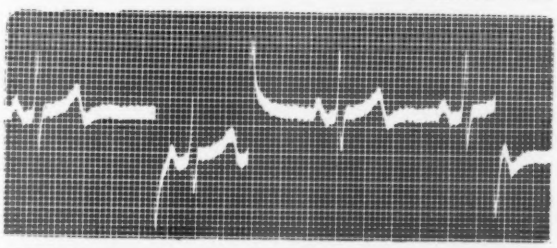
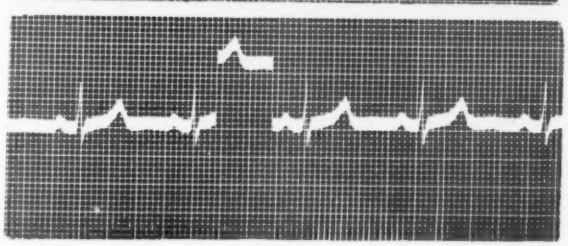


Fig. 3.



The added resistance of a patient in circuit or polarization of the electrodes may, however, so affect the characteristics of the string that its deflections are distorted, thus rendering certain features of the record impossible to interpret.

If nonpolarizable electrodes are used, the presence of high skin resistance may require loosening of the string to such an extent that it becomes overdamped and all its rapid deflections slurred (Fig. 1). If polarization of the electrodes is present, the string will overshoot, and the complexes may be considerably distorted from

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this cause (Fig. 2). When nonpolarizable electrodes are used, tracings obtained from patients offering low skin resistance show complexes not significantly distorted (Fig. 3).

Many methods have been advocated in an effort to provide a simple yet adequate contact between patient and electrode. The most acceptable of these methods is cumbersome, not adapted to leads from the chest, and entirely inadequate in occasional cases. Thus this problem has remained as a chief technical difficulty in clinical electrocardiography.

To avoid distortion it seems necessary: (1) to provide an electrode which will not polarize even in the presence of moderately high skin resistance; or, (2) to adjust the damping of the string to prevent in part the overshooting; or, (3) to reduce the skin resistance to consistently low values.

After considerable experimentation the first method, which involves electrodes either complicated, expensive, or cumbersome, was definitely laid aside.

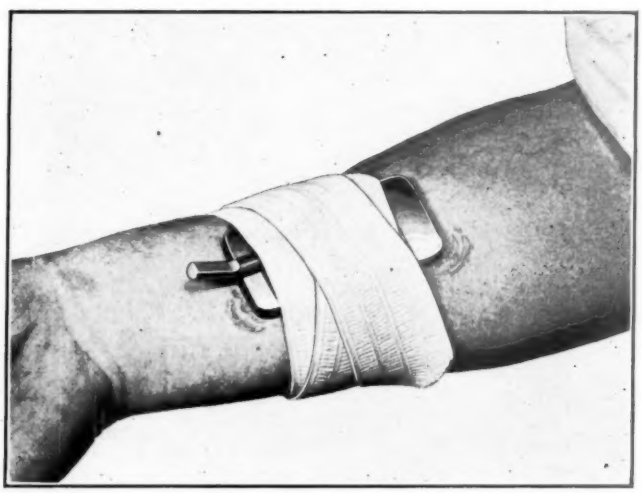

Fig. 4.

The second method seems open to criticism, for, as Lewis and Gilder[1] have shown, the deflection time of the string should be at least as low as 0.02 second when a resistance of 4,000 to 10,000 ohms is added to the circuit; otherwise the frequency response of the string may be below that of the oscillations to be recorded.

Experiments were then made with a view toward lowering sufficiently the natural impedence to electrical currents found in the skin, thus permitting the use of a high-frequency string of low resistance. By this procedure there would also be the added advantage of minimizing the effects of outside vibration. During the course of experimentation a combination of substances which gave unexpectedly good results was discovered, and it was found possible to include the requisite substances in the form of a paste. Using this paste, patients from whom it was previously impossible to obtain satisfactory electrocardiograms now yielded complexes of correct form and amplitude.

Although the chief purpose of the paste is to reduce skin resistance, it was found, moreover, to form an excellent nonpolarizing contact between skin and electrode.

In its initial form the mixture contained:

Sodium chloride	6½ lb
Pumice (powder)	8 lb.
Gum tragacanth	8 oz.
Potassium bitartrate	4 oz.
Glycerin	24 oz.
Carbolic acid	1 oz.
Water	2 gal.

The gum tragacanth and glycerin are heated in half the volume of water for six hours. The potassium bitartrate and sodium chloride are dissolved in the remaining volume of water and added. The resulting mixture is stirred thoroughly with an electric mixer and heated again for an hour. The carbolic acid and pumice are now added, together with more water if necessary, and the whole again mixed until of a creamy consistency.

In actual use a small quantity of the paste is rubbed briskly onto the desired skin area leaving a small surplus to facilitate contact with the electrode. The electrode, a german silver plate about 5 by 8 cm., is firmly applied over this area and held by means of an elastic ribbon or band (Fig. 4). The patient usually notices a slight burning sensation, but none has complained of any pain or discomfort. While no instance of skin irritation from this paste has occurred in a large number of patients, the usual caution should be observed with anyone having extremely sensitive skin.

Within reasonable limits, the size of the electrode is immaterial so far as skin resistance and polarization of the electrode are concerned. Resistance measured on the electrocardiograph, using the above electrodes and paste, is, in most cases, about 1,000 ohms and rarely as high as 2,000 ohms. This applies equally to myxedematous, cachectic or negro patients from whom it is sometimes difficult or impossible to obtain satisfactory tracings. Electrocardiographic tests made on patients in the wards of the Massachusetts General Hospital (about 400 cases) showed very uniform results, with resistances of from 1,000 to 2,000 ohms and no overshooting.

CONCLUSION

A new and simple procedure is outlined for avoiding distortion in taking standardized electrocardiograms. This consists of a new type of contact paste used with small metal electrodes.

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Department of Reviews and Abstracts

Selected Abstracts

Barnes, Arlie R.: Electrocardiogram in Myocardial Infarction. Arch. Int. Med. 55: 457, 1935.

A knowledge of the coronary blood supply of the left ventricle is essential to an understanding of the problem of acute coronary occlusion. It is essential to bear in mind that acute infarction involving the posterior basal portion of the left ventricle is approximately as common as is infarction of the anterior apical portion of that ventricle.

It is the situation of the acute infarct in the left ventricle and not the vessel supplying the area that determines the character of the electrocardiographic changes that will result.

Experimental ligation of vessels to the right and left ventricles of the dog produces electrocardiographic evidences of myocardial infarction that differ distinctly. Destruction of areas in the anterior portion of the left ventricle of the cat and of the dog produces electrocardiographic changes that are quite different from those obtained by the injury of similar portions of the posterior portion of the heart. The characteristic feature of these electrocardiographic changes is a deviation of the RS-T segment.

Care must be exercised in interpreting the results of experimental ligation of coronary vessels to distinguish between the changes in the electrocardiogram produced by the pericardial reaction and those attributable to actual infarction of the myocardium.

The preponderance of evidence is against the interpretation that deviation of the RS-T segment in acute myocardial infarction depends on the development of an additional factor of cardiac failure. Experimental and clinical evidence indicates that the RS-T deviation observed in the electrocardiogram after infarction is the primary event and that T-wave changes are sequential and secondary to that deviation. There is a definite pattern of RS-T changes characteristic of infarction in the anterior apical portion of the left ventricle and another indicative of infarction in the posterior basal portion of the left ventricle in the heart of man.

Although a constantly changing electrocardiogram observed after what is presumed to be acute coronary occlusion may be important corroborative evidence of that event, the degree with which these electrocardiographic changes approximate the T_1 or T_3 pattern will largely determine their worth in establishing the diagnosis of acute coronary occlusion.

Typically developed Q_1 and Q_3 patterns of infarction have a definite diagnostic and localizing value, and the combined consideration of the Q and T patterns will yield more information in the diagnosis than will either pattern considered alone.

Under proper conditions, the presence and situation of acute infarction can be predicted almost always from the electrocardiographic changes that develop. When changes in the electrocardiogram characteristic of acute myocardial infarction fail to develop, it will be found usually that tracings were not obtained in sufficient num-

ber or in proper time relation to the acute occlusion, that multiple acute infarctions of the left ventricle were present, that bundle-branch block obscured the changes, that pericarditis or pericardial effusion modified the electrocardiographic changes, or that the tracing was made at about the time of death.

Presumptive evidence of previous occlusion may be obtained from the appearance of inverted T-waves observed months after the acute occlusion. These T-waves are the coronary T-waves of Pardee and are chiefly characterized by their depth and the character of the R-T intervals that precede them. The reciprocal relation of T_1 and T_3, in which as one becomes more inverted the other becomes more positive, is important evidence of preceding acute occlusion.

By no means are all RS-T changes observed in angina pectoris, coronary sclerosis, or myocardial fibrosis to be ascribed to coronary disease. Many cases of angina pectoris, coronary sclerosis, and myocardial fibrosis present no significant electrocardiographic changes.

Neither the presence nor the situation of chronic cystrophic fibrosis of the myocardium is disclosed by any electrocardiographic change described to date.

Electrocardiograms with low voltage of the QRS complex in all leads after acute infarction probably increase the gravity of the prognosis.

The development of highly characteristic electrocardiograms of the T_1 or T_3 type after acute infarction seems to indicate a more favorable prognosis than do atypical electrocardiograms.

Electrocardiographic changes signifying acute infarction may appear as early as from one to two hours after acute coronary occlusion, and the electrocardiogram may not return completely to normal in some instances for two or three years or more.

Carter, J. Bailey, and Traut, Eugene F.: Quinidin and Strychnin in the Treatment of Premature Contractions. Am. J. M. Sc. **189:** 206, 1935.

In a cardiac patient, aged sixty years, with frequent ventricular extrasystoles, quinidine and strychnine together gave the greatest freedom from extrasystoles and from symptoms. Under these two drugs, his compensation improved; with them, with strychnine or quinidine separately, with iodide, and especially with digitalis, the extrasystoles increased in frequency, and his condition was correspondingly worse.

Sixteen of twenty patients with mild cardiac decompensation due to extrasystoles, when treated similarly with a combination of quinidine and strychnine, showed a favorable response.

Arnold, Harry, L., Middleton, William S., and Chen, K. K.: The Action of Thevetin, A Cardiac Glucosid, and Its Clinical Application. Am. J. M. Sc. **189:** 193, 1935.

Thevetin, a cardiac glucoside, has been isolated from the be-still nuts, and its physical, chemical, and pharmacological properties established. Of particular promise is its digitalis-like action. By biological assay its potency has been fixed as one-seventh that of ouabain. It is likewise one-seventh as toxic. Its action is more prompt and less sustained than digitalis. These facts serve as guides to its possible clinical applications and limitations.

The clinical trial of thevetin and other preparations of the be-still nuts in a group of twenty-three patients suffering from cardiac decompensation has justified certain deductions:

1. Thevetin and other preparations of the be-still nuts slow the heart rate in the presence of the normal conduction mechanism or of auricular fibrillation. In a single

case of auricular paroxysmal tachycardia, no reduction of the cardiac rate attended the use of thevetin.

2. Electrocardiographic studies of patients receiving these preparations closely parallel the results of digitalis therapy. Lengthening of the P-R interval, inversion of the T-wave, deviations of the S-T segments and alterations in the QRS complexes are characteristic.

3. Compensation is restored and maintained in appropriate cases of congestive heart failure. Diuresis occurs in the course of this altered circulatory balance.

4. In the clinical use of thevetin more or less serious conduction faults may develop occasionally, even though every reasonable precaution has been exercised. This hazard may be minimized if the potency and the comparative strength of this glucoside be borne in mind when it is used alone or in combination with drugs of similar action.

5. The irritant qualities of thevetin apparently deny its availability for intramuscular use.

6. The intravenous administration of thevetin has not been attended by evidence of local irritation or thrombosis.

7. Thevetin affords an added reliable and potent cardiac glucoside for intravenous use.

8. Extended study is necessary to determine the value of pure thevetin for oral use. The galenical preparations of defatted kernels, such as the tincture and the powder, appear to be clinically unsuitable because they frequently cause gastrointestinal disturbances, such as cramps and diarrhea.

Ginsberg, A. M., Stoland, O. O., and Loy, David T.: Studies on the Coronary Circulation. III. Effect of Intravenous Injections of Dextrose on the Coronary Circulation. Arch. Int. Med. **55**: 42, 1935.

The effect of intravenous administration of dextrose on the coronary circulation has been determined on the intact animal and on denervated and innervated heart-lung preparations before and after cutting of the vagus nerves.

Intravenous injection of 5 gm. of dextrose in a 50 per cent solution produced a marked and sustained increase in the coronary circulation of the intact dog under ether anesthesia. Hypertonic solution of dextrose in amounts equivalent to that used in the intact animal produces no significant change in the the coronary flow of denervated or innervated heart-lung preparations. Repeated injections of dextrose are effective in increasing the coronary flow of intact animals.

Part of the increase in the coronary flow can be accounted for by the increased water content of the blood, the water being drawn mainly from organs other than the heart and lungs. That the increased flow is not due to a reflex involving the nerve centers is evidenced by the fact that in the innervated heart-lung preparations no increase in the coronary flow followed injections of dextrose.

The sustained increase in the coronary flow in the intact animal and the absence of undesirable physiological reactions following the administration of hypertonic solutions of dextrose may account for many favorable clinical results reported and also suggest its use as a therapeutic agent for patients requiring improvement in the coronary circulation.

Elliot, A. H., and Nuzum, F. R.: Cardiovascular Response to the Subcutaneous Injection of Epinephrin and Pituitrin in Essential Hypertension. Am. J. M. Sc. **189**: 215, 1935.

The blood pressure and pulse rate were measured at five-minute intervals over a sixty-minute period in thirty-two individuals with essential hypertension who had received a subcutaneous injection of 1 mg. of epinephrine.

The average systolic pressure fell slightly over a period of thirty-five minutes and then returned to the preinjection level; the average diastolic pressure fell to a maximum low point at forty-five minutes and remained near that level throughout the remainder of the period. The average pulse pressure decreased. The average pulse rate rose.

A degree of parallelism existed between changes in the systolic pressure and in the pulse rate of these patients, such that a rise in pressure was usually accompanied by a rise in pulse rate and a fall in systolic pressure may be primarily the result of cardiac stimulation by epinephrine, whereas, the fall in diastolic pressure is attributable to arteriolar dilatation.

In forty hypertensive patients studied in a similar manner after receiving a subcutaneous injection of pituitrin, a slight rise in average diastolic pressure and an equally slight fall in average systolic pressure were observed after twenty minutes. The average pulse rate was unchanged.

In the same patient an unusual response to the injection of pituitrin was not necessarily accompanied by a vigorous response to epinephrine.

No constant or frequent deviation from the reported normal cardiovascular response to the subcutaneous injection of epinephrine and pituitrin could be demonstrated in this series of patients with essential hypertension.

Katz, Louis N., and Landt, Harry: The Effect of Standardized Exercise on the Four-Lead Electrocardiogram. Am. J. M. Sc. **189**: 346, 1935.

Exercise tests were carried out in twenty patients having a history of angina pectoris on effort. The effect of the test on the four-lead electrocardiogram and on the development of angina was correlated with the appearance of the electrocardiogram at rest. The majority of the patients had abnormal electrocardiograms of varying degrees. Only four had four-lead electrocardiograms within normal limits. Lead IV was never found to be abnormal when the other three leads were normal, but the reverse was true in many patients.

One precaution was found to be essential, namely, to stop the exercise when generalized fatigue, dyspnea, cyanosis or anginal pain appeared before the time for the test was up.

The appearance of the four-lead electrocardiogram taken at rest, the effect of a standardized exercise on the four-lead electrocardiogram, and the effect of such an exercise in producing anginal attacks are to be regarded as a triad which together augment the knowledge of the condition of the coronary circulation, obtained from clinical examination alone. The fact that positive findings by one of these three criteria can occur with negative findings by the other two shows the value of relying on a combination of all three, rather than on any one of them alone. There can be no doubt that the fourth lead is a valuable addition to the other leads in carrying out this analysis.

Muir, D. C., and Brown, J. W.: Congenital Heart Disease. Brit. M. J. **1**: 966, 1935.

These remarks are based on observations and investigations of a series of cases numbering over 200, during a period of some years. The cases are described in two groups, those without and those with cyanosis. The remarks relate to the underlying anatomical conditions which produce the various physical signs observed in the patients. Diagnostic signs are discussed. It is shown that in most instances satisfactory antemortem diagnoses may be made.

Proger, S. H., and Minnich, W. R.: Left Axis Deviation With and Without Heart Disease. Am. J. M. Sc. **189:** 674, 1935.

Electrocardiograms showing left axis deviation with no other abnormal findings were analyzed with particular reference to the presence or absence of a relatively low erect T-wave in Lead I, a prominent S-wave in Lead II, and an erect T-wave in Lead III.

The analysis indicates that in the absence of any of the three changes above enumerated the left axis deviation is not associated with cardiovascular disease. In the presence of one of the changes the incidence of associated cardiovascular disease is considerable, in the presence of two changes it is greater, while the presence of all three changes constitutes almost invariable evidence of heart disease.

Observations of repeated electrocardiograms taken over periods varying from seven months to four years show the development of these associated changes in the presence of progressive cardiovascular disease.

Richter, Harry A.: Value of Serial Electrocardiograms in Coronary Thrombosis. Am. J. M. Sc. **189:** 487, 1935.

An attempt has been made to show the value of serial curves in the diagnosis of coronary thrombosis. It is possible for single records to be taken at times when characteristic signs of coronary thrombosis are absent. The serial records are usually characteristic and rule out those conditions simulating coronary occlusion curves in a single record, such as seen in chronic valvular disease, hypertrophied hearts of athletes, and those of chronic coronary disease. The serial curves of acute infectious diseases usually are not characteristic enough to confuse the diagnosis. In an occasional case it may be necessary to rely upon the correlation of the clinical history and findings with the electrocardiogram.

The time of taking these curves for practical purposes has been suggested, i.e., as soon as possible after the accident; then, the next day; forty-eight hours after the second; and, if necessary, at weekly intervals for a month or longer.

It may be that chest leads will further increase the accuracy of serial curves. In the experience of the author, the fourth lead has been more sensitive to digitalis than the conventional leads.

In seventy-two cases of coronary thrombosis in which serial curves were taken, only two failed to show significant changes.

Sprague, Howard B., and Orgain, Edward S.: Electrocardiographic Study of Cases of Coronary Occlusion Proved at Autopsy at the Massachusetts General Hospital, 1914-1934. New England J. Med. **212:** 903, 1935.

The study here presented reports the autopsy experience at the Massachusetts General Hospital for twenty years (1914-1934) in proved cases of coronary occlusion in which electrocardiographic records had been made shortly before death. Sixty-one cases are analyzed. Complete or recanalized thrombosis of a main artery or a main branch was found in the left coronary system in forty-six cases and in the right in twenty-one cases. In the same period of time 437 cases of coronary occlusion have been diagnosed clinically in the hospital.

It is clear that cases with acute coronary thrombosis with closure limited to a single coronary artery or branch of an artery are relatively rare at the autopsy table. Only seventeen cases are so designated in this series, and not all of these were completely uncomplicated. The development of the Q_1T_1 and the Q_3T_3 changes in this group is most typical, and it is this change in the electrocardiogram which is specific for the localization of myocardial infarct. Inversion of

the T-waves alone may be seen in all leads in pericarditis, rheumatic carditis, uremia, in rare and unexplained cardiac disease in which the coronary system is normal at autopsy and apparently in relation to anoxemia and possibly coronary spasm as a temporary phenomenon.

When acute cardiac infarction is limited to the apex and anterior wall of the left ventricle, the authors' figures indicate an accuracy of 70 per cent in the localization of the infarct by the electrocardiogram from standard limb leads. In posterior or diaphragmatic infarcts or infarcts of the right ventricle, the electrocardiogram was typical and diagnostic in only 30 per cent, but this was influenced by the presence of intraventricular block, and the series was small. It appears likely that more careful study with serial electrocardiograms and precordial leads will improve these figures although as yet the use of precordial leads appears of more value in localizing anterior rather than posterior infarcts. The occurrence of intraventricular block is a serious handicap to accurate antemortem localization of infarcts in the myocardium, but in some instances repeated tracings are of value in diagnosing the advance of the occlusion or the development of a fresh one. Apparent inconsistencies between the pathological and electrocardiographic findings should lead at necropsy to a more careful study of all parts of the myocardium, even when the position of the fresh infarct seems obvious. However, high degrees of coronary thrombosis with fresh infarction can occur with normal electrocardiograms. In the three cases in this series, the infarction was in the posterior wall of the left ventricle in two and diffusely over the endocardium of the left ventricle in one.

In the group of sixteen cases with old and fresh occlusion, low voltage and intraventricular block become more prominent (eleven cases), and the T-wave changes less typical. In this series, only one case of the T_1 type appeared and this was not entirely characteristic. Eight cases of the T_3 type were recorded, but apparently there was no more relationship to the fresh infarct than to the older process, and in one case no infarct was found but the right coronary ostium was closed by a luetic process in the aorta. In this group, also, a case was found with occlusion of all the main coronary branches without myocardial infarction with normal electrocardiogram three weeks before death.

The final group of twenty-eight, with old coronary and myocardial pathological conditions, consists of cases, many of which were diagnosed as coronary thrombosis only at autopsy, although angina pectoris was the presenting symptom in thirteen, cardiac asthma in twelve, and dyspnea on exertion in two. Congestive failure was a frequent cause of death. In only eight cases were the electrocardiograms characteristic either of anterior or posterior cardiac infarction. Intraventricular block was present in eight cases and low voltage, in five. T-wave changes of an indefinite nature occurred in eight. It was clear by electrocardiogram that myocardial disease based on coronary arteriosclerosis was present in all but two cases, and in these two the clinical history revealed prolonged angina pectoris; but little hope of localizing the cardiac infarct could be expected from a study of this group. However, had serial electrocardiograms been taken for several years before death, the position of some of these infarcts might very well have been deduced. In the entire group of forty-four cases showing old coronary occlusion with or without fresh occlusion, the electrocardiogram was diagnostic of cardiac infarct, irrespective of its location, in 38 per cent.

This study is intended to summarize the situation in relation to coronary thrombosis in a general hospital in which there has been an active interest in the problems of coronary disease for many years but in which no special technics have been used for demonstrating coronary and myocardial pathology at autopsy. It illustrates what can be expected in the routine work of the electrocardiographic

laboratory and autopsy room, and it points the way toward more intensive study by both departments in order to ultilize the material which may be available in the future for the solution of the problems of diagnosis and prognosis still remaining in this condition.

Wedd, Alfred M., and Smith, R. Eloise: Observations on Prognosis in Angina Pectoris. Am. J. M. Sc. **189:** 690, 1935.

A study was made of 166 cases of effort angina, seen in a clinic in which arteriosclerotic heart disease is the predominant type. The influence of hypertension, obesity, familial vascular disease, and certain miscellaneous factors has been considered. Electrocardiograms were available for most patients but were found of no value for prognosis. Nearly one-third of these patients died suddenly, and over half died from coronary occlusion. Cardiac or vascular disease was responsible for death in over 80 per cent of the series. The average duration of life in this series, 5.8 years, was greater than is usually anticipated. While prognosis in the individual case must always be uncertain, when viewed in the light of its comparatively long duration, and the late ages at onset and death, compared with life expectancy, the anginal syndrome appears less grave and does not stand out as a serious complication of arteriosclerotic heart disease, with which it is most commonly associated.

Robertson, Harold F., and Fetter, Ferdinand: The Effect of Venesection on Arterial, Spinal Fluid, and Venous Pressures with Especial Reference to Failure of the Left and Right Heart. J. Clin. Investigation **14:** 305, 1935.

A series of experiments was carried out to determine the relation of arterial, spinal fluid, and venous pressures before and after venesection.

It was found in right heart failure that venous and spinal fluid pressures were elevated and related with respect to fall of pressures induced by venesection. The variation of the ratio between the two pressures is shown by the divergences from a linear distribution.

The spinal fluid pressure was elevated above normal in 32 per cent and 85 per cent of left and right heart failures, respectively. No correlation obtained between the arterial blood pressure and the venous or spinal fluid pressures in either right or left cardiac incompetence. The venous and spinal fluid pressures were uncorrelated in failure of the left heart. The spinal pressure was greater than the venous pressure in all of 140 observations made on thirty-five patients.

Cassio, P., and Orias, O.: Snap of the Mitral Orifice. Rev. argent. de cardiol. **1:** 450, 1935.

A phonocardiographic study of seventeen cases of mitral stenosis showed that the extra sound for each cardiac cycle occurred at the moment when the isometric relaxation ends and the ventricular inflow begins, i.e., at the moment of opening of the A-V valves. The term "opening snap," which this extra sound has received, is produced by diseased conditions in the mitral valve and is justified in its time relation with the cardiac events. Its separation from the second sound depends on the duration of the isometric relaxation phase and bears a certain relationship to the heart rate.

When present, this characteristic auscultatory sign of mitral stenosis has a considerable diagnostic value. It also persists after auricular fibrillation develops, when the murmurs usually disappear. The fact that the extra sound may vary over different precordial areas, from the left of the sternum to the apex region, does not mean, so far as the evidence gathered from this study is concerned, a different mechanism for its production.

In order to interpret correctly the significance of a supposed opening snap of the mitral valve when graphic methods are used, it is necessary to record the heart sounds simultaneously with the optical venous pulse. Otherwise it is impossible to determine accurately the exact moment of occurrence of the phonocardiographic accidents and, consequently, to distinguish the opening snap from a doubling of the second sound or from any other of the sounds which occur early during diastole under normal or pathological conditions.

Bramwell, Crighton: Gallop Rhythm. Quart. J. Med. 4: 149, 1935.

Presystolic gallop is a sign of great clinical significance, and, for this reason alone, it should be clearly distinguished from all other types of triple rhythm.

Gallop rhythm occurs most frequently in patients with hypertension, advanced coronary disease, or acute inflammatory lesions of the heart. It is an extremely grave sign in prognosis. Very few patients live for more than two years after gallop rhythm develops. True gallop rhythm is not casually related to A-V block nor to bundle-branch block. Auricular contraction, tachycardia, and a failing heart are the factors essential to the production of gallop.

It is suggested that the additional impulse in gallop rhythm is produced by sudden distention of the ventricle and the additional sound, by vibrations of the ventricular wall, both these phenomena being due to an abnormally rapid rate of filling of the ventricle when the myocardium is lacking in tone.

Bramwell, Crighton: Sounds and Murmurs Produced by Auricular Systole. Quart. J. Med. 4: 139, 1935.

Records of the heart sounds in a case of Graves' disease with partial heart-block show that the initial vibrations of the first heart sound in normal cycles bear the same time relation to the P-wave in the electrocardiogram as do the vibrations of the auricular phonogram to the blocked auricular beats. These two series of vibrations are also similar in form.

When the P-R interval is prolonged, the complete series of vibrations in the auricular phonogram precedes the larger vibrations of the ventricular phonogram; but when the P-R interval is of normal duration, the two series of vibrations overlap.

These observations prove that in this case the initial vibrations of the first heart sound are produced by the auricle and not by the ventricle. It is suggested that the initial vibrations seen in records obtained from normal subjects may also be attributable to auricular systole. These initial vibrations are, however, usually of such small amplitude that they fail to reach the threshold of audibility.

It is suggested that the similarity between the first heart sound in hyperthyroidism, in certain athletes, in some cases of congenital heart disease, and in some patients with high blood pressure, on one hand, and the first heart sound and presystolic murmur of mitral stenosis, on the other hand, may be due to an increased velocity of the blood flow through the mitral orifice when the auricular muscle is hypertrophied.

The late development of the auricular sound suggests that it is not entirely due to a muscle tone but in part at least to vibrations set up by the blood ejected by the auricle.

Records of heart sounds and murmurs in two cases of mitral stenosis complicated by partial heart-block showed that the time relations of the auriculosystolic element of the mitral murmur were strictly analogous to those of the auricular component of the first heart sound in the case of hyperthyroidism described.

There is a striking variation in the intensity of the auriculosystolic murmur in different cycles of these records. When auricular systole occurs early in diastole, the murmur is loud; but when it occurs at the end of a prolonged diastole, it may be so faint that it fails to reach the threshold of audibility. Its absence in cycles following a blocked auricular beat is explained by the inability of the engorged ventricle to accept the auricular output.

It is suggested that summation of the terminal vibrations of the auriculosystolic murmur and the initial vibrations produced by ventricular systole may account for the accentuation of the first heart sound in patients with mitral stenosis.

Wilson, May G., Ingerman, Eugenia, DuBois, Robert O., and Spock, Benjamin McL.: The Relation of Upper Respiratory Infections to Rheumatic Fever in Children. I. The Significance of Hemolytic Streptococci in the Pharyngeal Flora During Respiratory Infection. J. Clin. Investigation 14: 325, 1935.

There are presented investigations conducted over a period of several years comprising epidemiological, bacteriological, and clinical studies of a large group of rheumatic children observed in the homes, hospital wards, and convalescent cottages.

Two hundred twenty-two ambulatory rheumatic subjects from five to fifteen years old experienced 783 respiratory infections and 401 rheumatic recurrences (for a two-year period of observation, 1930 to 1932). Less than 10 per cent of the rheumatic attacks were preceded within three weeks by a respiratory infection.

Of a total of 123 rheumatic subjects under close observation for twelve months, September, 1933, to September, 1934, 98 per cent suffered 649 attacks of respiratory infection, of which 353 were associated with the presence of hemolytic streptococci in the throat flora. Eighty-four per cent of the respiratory infections were not associated with rheumatic activity.

Forty-nine per cent of the subjects experienced 139 rheumatic episodes; a quiescent interval, subsequent to "streptococcal" respiratory infection, preceded 11.5 per cent of the rheumatic episodes.

Sixty-two rheumatic subjects were under daily observation at the convalescent cottages for a two-to-twelve-month period. During three epidemics of respiratory infection associated with a predominance of hemolytic streptococci in the pharyngeal flora, there was no appreciable increase of rheumatic activity.

Rheumatic subjects experienced an average of five attacks of respiratory infection as compared with an average of three for the nonrheumatic children of their respective households.

During the spring of 1934 hemolytic streptococci appeared in the pharyngeal flora of the majority of the rheumatic and nonrheumatic subjects.

During this season of its highest incidence, hemolytic streptococci predominated in the pharyngeal flora of 50 per cent of the rheumatic subjects during health, 40 per cent during respiratory infections, and 10 per cent during rheumatic activity.

The evidence presented does not support the conception of a specific etiological relationship between respiratory infections and rheumatic fever in children.

The authors' observations would tend to minimize the diagnostic significance of the presence or absence of hemolytic streptococci in the pharyngeal flora during respiratory infections. The designation streptococcal respiratory infection, based solely on bacteriological findings, would not appear to be justified.